

ANNALS of SURGERY

A MONTHLY REVIEW OF SURGICAL SCIENCE AND PRACTICE

Also the Official Publication of the American
Surgical Association, the Southern Surgical
Association, Philadelphia Academy of
Surgery, and New York Surgical Society

VOLUME 110

JULY—DECEMBER

1939

J B LIPPINCOTT COMPANY, Publishers

PHILADELPHIA

MONTREAL

LONDON

NEW YORK

COPYRIGHT 1939

J B LIPPINCOTT COMPANY

MADE IN THE UNITED STATES OF AMERICA

CONTRIBUTORS TO VOLUME 110

	Page
ABBOTT, LEROY C , San Francisco, Calif	961
ALLEN, A W , Boston, Mass	693
BAILEY FRED W , St Louis, Mo	149
BALFOUR, DONALD C , Rochester, Minn	790
BARKER, M HERBERT, Chicago, Ill	1016
BARROW, D WOOLFOLK Lexington, Ky	1118
BARTLETT, WILLARD, St Louis, Mo	156
BAXTER, JR JAMES H , Nashville Tenn	84
BEECHER, HENRY K Boston, Mass	823
BERNHARD, A , New York, N Y	701
BEST, R RUSSELL, Omaha Neb	67
BINNEY, HORACE, Boston, Mass	578
BISGARD, J DEWEY Omaha, Neb	802
BLAIR, VILRAY P , St Louis, Mo	151
BLALOCK, ALFRED, Nashville, Tenn	544
BOLDREY EDWIN B , Montreal, Canada	273
BOURNE WESLEY, Montreal, Canada	830, 872
BROWDER, JEFFERSON, Brooklyn, N Y	357
BROWN, W EASSON, Toronto, Canada	863
BUCHANAN, EDWIN P , Pittsburgh, Pa	140
BUSH, LEONARD F , Danville, Pa	851
CAMPBELL, WILLIS C , Memphis, Tenn	119
CARP, LOUIS, New York, N Y	107
CARTER, BURR N , Cincinnati, Ohio	562
CHERNEY, LEONID S , San Francisco, Calif	316
CLARK, DWIGHT E , Chicago, Ill	907
COLP, RALPH, New York, N Y	648, 795
CORWIN, WARREN C , Rochester, Minn	461
DANDY, WALTER E , Baltimore, Md	161
DARRACH, WILLIAM, New York, N Y	948
DAVIS, LOYAL, Chicago, Ill	1016
DENNIS, CLARENCE, Minneapolis, Minn	629
DERBY, IRVING M , Brooklyn, N Y	480
DRAGSTEDT, LESTER R , Chicago, Ill	907
EGGERS, CARL, New York, N Y	797
ELKIN, D C , Atlanta, Ga	169
ELKINTON, J RUSSELL, Philadelphia, Pa	1050
ELOESSER, LEO, San Francisco, Calif	786
ELTING, ARTHUR W , Albany, N Y	792
ELVIDGE, ARTHUR R , Montreal, Canada	273
ESSER, JOHANNES F S , Monaco	311

	Page
FARMER, ALFRED W , Toronto, Canada	951
FINE, JACOB, Boston, Mass	25, 411
FINLAYSON, ALISTER I , Omaha, Neb	67
FITZGERALD, R R , Montreal, Canada	81
FITZHUGH, O GARTH, Nashville, Tenn	84
FLOOD, CHARLES A , New York, N Y	37
FOOTE, MERRILL N , Brooklyn, N Y	158
FOSS, HAROLD L , Danville, Pa	851
GARLOCK, JOHN H , New York, N Y	474
GENDEL, SAMUEL, Boston, Mass	25, 411
GERBODE, F , San Francisco, Calif	669
GERSTER, JOHN C A , New York, N Y	389
GILMOUR, MONROE T , Philadelphia, Pa	1050
GINZBURG, LEON, New York, N Y	648
GOLDMAN, LEON, Chicago, Ill	755
GRAHAM, CHARLES P , Wilmington, N C	285
GRAHAM, EVARTS A , St Louis, Mo	1115
GRAHAM, ROSCOE R , Toronto, Canada	863
GRANT, FRANCIS C , Philadelphia, Pa	488
GRODINSKY, MANUEL, Omaha, Neb	177
GROSS, ROBERT E , Boston, Mass	321
GURD, FRASER B , Montreal, Canada	872
HALFORD, F J , San Francisco, Calif	669
HAMSA, WILLIAM R , Omaha, Neb	447
HANFORD, JOHN M , New York, N Y	131
HARRIS, ROBERT I , Toronto, Canada	1095
HART, DERYL, Durham, N C	291, 916
HARTMAN, F W , Detroit, Mich	835
HARVEY, HAROLD D , New York, N Y	1067
HAWKES, STUART ZEH, Newark, N J	466
HEINBECKER, PETER, St Louis, Mo	1037
HELWIG, FERDINAND C , Kansas City, Kans	682
HICKEN, N FREDERICK, Omaha, Neb	67
HINTON, J WILLIAM, New York, N Y	376
HODGE, EDWARD B , Philadelphia, Pa	160
HOLDER, HALL G , La Jolla, San Diego, Calif	94
HORRAX, GILBERT, Boston, Mass	513
HORSLEY, J SHELTON, Richmond, Va	606
HUGGINS, CHARLES, Chicago, Ill	940
HUNNER, GUY L , Baltimore, Md	231
HUNT, VERNE C , Los Angeles, Calif	622
IVY, A C , Chicago, Ill	755
JACKSON, REGINALD H , Madison, Wis	14
JOHNSON, E K , Omaha, Neb	802
JONES, JR , RANDOLPH, Durham, N C	916
KENT, EDWARD M , Norwich, Conn	659
KLEINBERG, SAMUEL, New York, N Y	144

	Page
KOHN, IRVING L , New Yoik, N Y	701
KRUSEN, FRANK H , Rochestei, Minn	417
LAHEY, FRANK H , Boston, Mass	I
LEAMAN, WILLIAM G , Philadelphia, Pa	766
LEHMAN, EDWIN P , Univeisity, Pa	153
LOEB, SAM A , Sweetwater, Texas	314
LUNDY, JOHN S , Rochestei, Minn	878
MACGUIRE, JR , CONSTANTINE J , New Yoik, N Y	472
MACKAY, EATON M , La Jolla, San Diego, Calif	94
MACLACHLIN, ANGUS, Toionto, Canada	1095
MARTIN, JR , J D , Atlanta, Ga	169
MASON, M F , Nashville, Tenn	544
MCCLURE, ROY D , Detioit, Mich	835
MCQUEENEY, ANDREW M , Bridgeport, Conn	50
MEIGS, JOE VINCENT, Boston, Mass	731
MELENEY, FRANK L , New Yoik, N Y	1067
MEYERDING, HENRY W , Rochester, Minn	417
MEYERS, RUSSELL, Brooklyn, N Y	357
MILLER, EDWIN M , Chicago, Ill	587
MITCHELL, CHARLES F , Philadelphia, Pa	160
MOCK, HARRY E , Chicago, Ill	464
MOON, VIRGIL H , Philadelphia, Pa	260
MORGAN, HUGH J , Nashville, Tenn	544
NEWELL, E DUNBAR, Chattanooga, Tenn	100
NORCROSS, NATHAN C , Philadelphia, Pa	488
ORNDORFF, JOHN R , Chicago, Ill	464
ORR, THOMAS G , Kansas City, Kans	682
PASTERNAK, JOSEPH G , New Orleans, La	427
PERRETT, T S , Toionto, Canada	1095
PREIFFER, DAMON B , Norwich, Conn	659
PHIEMISTER, DALLAS B , Chicago, Ill	481, 960
PICKHARDT, OTTO C , New Yoik, N Y	701
PILCHER, JAMES T , Brooklyn, N Y	320
POPPEN, JAMES L , Boston, Mass	513
PRESTON, ROBERT L , New York, N Y	800
RANKIN, FRED W , Lexington, Ky	380
REICHERT, F L , San Francisco, Calif	669
RIENHOFF, JR , WILLIAM FRANCIS, Baltimore, Md	886
RIVEN, S S , Nashville, Tenn	544
ROBBINS, BENJAMIN H , Nashville, Tenn	84
ROBERTSON, JAMES F , Wilmington, N C	285
RODMAN, J STEWART, Philadelphia, Pa	766
ROSENFELD, LOUIS, Boston, Mass	411
ROURKE, G M , Boston, Mass	693
SAUNDERS, JOHN B DEC M , San Francisco, Calif	961

	Page
SCHELLING, VICTOR, Detroit, Mich	835
SCHNEDORT, J G, Detroit, Mich	835
SCHOOLFIELD, BEN L, Dallas, Texas	437
SHELLEY, HAROLD J, New York, N Y	456
SINGLETON, ALBERT O, Galveston, Texas	525
SMYTH, JR, CALVIN M, Philadelphia, Pa	160
SPEED, J S, Memphis, Tenn	119
STEWART, J D, Boston, Mass	693
ST JOHN, FORDyce B, New York, N Y	37
SUSSMAN, MARCY New York, N Y	648
TAYLOR, EARL S, New York, N Y	200
THOMPSON, T CAMPBELL, New York, N Y	992
UPCHURCH, S E, Durham, N C	291
VERMEULEN, C, Chicago, Ill	907
VINEBERG, A M, Montreal, Canada	872
WANGENSTEEN, OWEN H, Minneapolis, Minn	629
WARREN, RICHARD, Boston, Mass	222
WAUGH, RICHEy L, New Orleans, La	427
WEEDER, S DANA, Philadelphia, Pa	55
WHITE, HARVEY L, St Louis, Mo	1037
WIEGE, EUGENE, Chicago, Ill	940
WILSON, CLYDE L, Jamestown, N Y	60
WILSON, PHILIP D, New York, N Y	992
WOLFF, WILLIAM A, Philadelphia, Pa	1050
WRIGHT, LOUIS T, New York, N Y	314
ZIEROLD, ARTHUR A, Minneapolis, Minn	723



CARCINOMA OF THE COLON AND RECTUM¹

DEDUCTIONS FROM EIGHT HUNDRED OPERATIONS

FRANK H LAHEY, M D

BOSTON, MASS

THE title of this paper was chosen in order that I might not be limited in it to the discussion of any one aspect of this disease, but rather so that I would be able to present deductions from our experiences with various aspects of the subject which might be of value to others who have perhaps not had the opportunity of dealing with these patients in such numbers

While everyone who is dealing with patients who have carcinomata of the colon and rectum is very conscious of their frequent origin in polypi and adenomata which are, on their first appearance, benign, altogether too little has been written and said concerning the relationship of polypi and adenomata of the large intestine to cancer. Those of us who are interested in this subject have preached and written on the need for earlier diagnosis of carcinoma of the large bowel, the relatively low grade of malignancy which these lesions show, and the high percentage of cures which can be obtained by radical surgical measures. We need, however, to call attention forcibly to the fact that since most cancers of the rectum and colon originate in lesions which are primarily benign and removable in their benign stage, the most important teaching which can be spread before the public, medical and lay, is the need for the diagnosis and removal of polypi and adenomata before they become malignant

When one realizes that 75 per cent of all the carcinomata occurring in the large bowel arise in the descending colon, sigmoid, rectosigmoid and rectum, that the statistics of M^r J H Saint show that 65 per cent of all the polypi occurring in the large bowel arise in the descending colon, sigmoid, rectosigmoid and rectum, one cannot avoid making the deduction that there is a distinct association between the two. One cannot avoid making comparison of the origin of carcinoma of the thyroid in adenomata which are primarily benign with the origin of cancer of the rectum in papillomata and adenomata which are likewise primarily benign, the removal of which, in both instances, while still benign is the desirable stage in which to attack potential carcinoma of the large bowel or potential carcinoma of the thyroid

When one realizes that most of the pathologic reports of specimens of carcinoma of the colon and rectum are either malignant adenoma or adeno-

* Read before the Southern Surgical Association, White Sulphur Springs, W Va, December 6, 7, 8, 1938

carcinoma, one likewise cannot avoid making a deduction of a possible association between this lesion and polyp and adenomata

When one visualizes typical lesions found in carcinoma of the colon and rectum spreading from a central point to a periphery with elevated edges, one cannot likewise again avoid making the deduction that such a carcinoma started in a lesion at a central point which was originally benign, only to become malignant and spread peripherally

When one further realizes the quite well established clinical maxim, that when a malignant lesion of the large bowel completely encircles the entire caliber of that structure it is from six months to one year old, one cannot avoid making the deduction that this lesion in the beginning started at a local point, probably from a polyp or adenoma, only to spread out peripherally and involve the entire lumen of the bowel

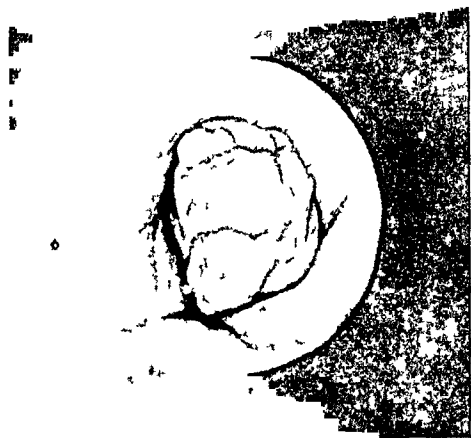


FIG 1—A rectal polyp seen through a proctoscope. This is an ideal polyp for fulguration and one can readily appreciate from this lesion how carcinoma may originate in it

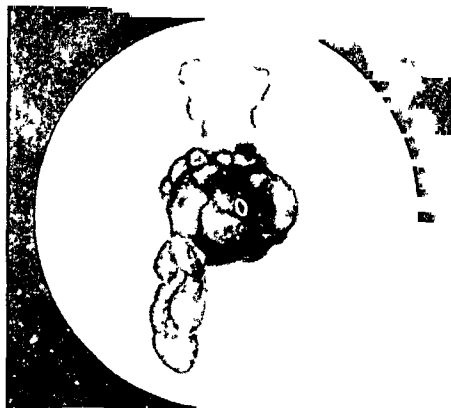


FIG 2—Polyp removed from the sigmoid by sigmoidotomy. This occurred in a doctor in whom there was a history of blood in the stools for a period of two years the cause never having been discovered. This was, however, finally demonstrated by contrast enema.

Pathologically it proved benign. Note the generous area of mucosal base removed.

All of the above deductions lead one to the conclusion that we must all be more diligent and painstaking in our search for polypi and adenomata in the presence of the passage of blood by rectum

While thorough proctoscopic, sigmoidoscopic and contrast barium enema examinations must be undertaken in the colons and rectums of all patients passing blood, there is an even greater necessity that routine proctoscopic and sigmoidoscopic examinations be made on all patients presenting themselves for physical examination for any condition whatsoever, no matter how unrelated it may be to a possible colon or rectal lesion. This is necessary, if we are to discover the largest possible number of polypi and adenomata before they have become malignant in character or very early in their stage of malignant degeneration, since many of these polypi and adenomata exist without the appearance of blood in the stools until they have become malignant in character. As evidence of the value of this routine procedure, it is of interest to state that with routine proctoscopic examinations made in the clinic,

only within the last two to three years, polypi and adenomata have been found and removed either by fulguation through the sigmoidoscope or proctoscope or by sigmoidotomy or colotomy in 250 patients. One cannot, of course, say that every one of these patients would have had a cancer of the rectum or colon, but again one cannot avoid making the deduction that by the removal of these adenomata, while still benign, a number of these patients have been saved from the later development of carcinoma of the rectum or colon.

The proper preparation of patients for sigmoidoscopy, by means of cleansing enemata and the proper tables for obtaining satisfactory position for proctoscopy and sigmoidoscopy, hardly requires mention. It is, however, of great importance to call attention to the greater satisfaction with which such examinations can be made with the patient hanging over the edge of the proper table so that the rectum hangs by its levator and anal attachments. When proctoscopic and sigmoidoscopic examinations are made in this position, liquid feces do not run into the examining instrument to occlude vision, and the walls of the suspended rectum and sigmoid adjust themselves readily to visualization of polypi, adenomata and malignancies arising in them.

As the result of our experience in fulgulating these polypi and adenomata, we would particularly call attention to the dangers associated with fulguation of high polypi and adenomata and the need of undertaking fulguation in such high lesions with the patient in the hospital where emergencies, should they arise, can be immediately dealt with. One can never be sure, in fulgulating polypi and adenomata high in the rectum and sigmoid, that uncontrollable bleeding will not occur. Should such a situation arise in a patient fulguated in one's office, valuable time and unnecessary blood is lost in transporting such an individual to a hospital for a necessary abdominal procedure to control such bleeding.

One does not need to discuss before this audience the value of contrast enemata in demonstrating large bowel adenomata and polypi while still in the benign stage and safely removable by colotomy. Roentgenologists should not forget the necessity of thoroughly cleansing the entire colon if one wishes to obtain good outline patterns of the mucosal lining of the colon. One cannot expect thin barium mixtures to adhere to the mucosal wall of the colon when that structure is filled with feces.

We are so constantly urged, both by patients and their family physicians, to perform local, nonmutilating operations by which the sphincter is preserved when the lesions are very small, that one of the important deductions which has resulted from this experience should be forcibly stated, that is, that in general, the smaller the lesion, if definitely proven to be malignant, the more aggressive should be the surgery, as the better is the chance for a permanent cure. One is a poor adviser if one permits himself to be persuaded by unwise patients and an uninformed family physician into performing a local operation on a small malignant lesion only to have the patient return for a radical operation in a state when the possibility of a cure is hopeless.

Dr. Neil W. Swinton has reviewed 100 proven cases of carcinoma of the

right colon, 100 proven cases of carcinoma of the left colon and 100 proven cases of carcinoma of the rectum, relative to their symptomatology (Table I)

TABLE I

ANALYSIS OF 300 CASES OF PROVEN CARCINOMATA OF THE LARGE BOWEL AT DIFFERENT LEVELS, RELATIVE TO THEIR SYMPTOMATOLOGY

	Rectum	Left Colon	Right Colon	Total
	100	100	100	300
	Per Cent			
1 Altered bowel function	79	82	81	80
2 Abdominal cramps or pain	7	77	87	57
3 Abnormal stools	86	47	9	46
4 None	2	2	3	2 3

When one realizes that out of these 300 cases of proven carcinoma of the large bowel at different levels, 97.5 per cent had an alteration in some form of bowel function, one wonders how it is possible to miss the diagnosis in these cases

While alteration of bowel function as an indication of the presence of a possible malignancy of the colon has been repeatedly preached and written about, there is still a lamentable lack of appreciation in the minds of lay people and many physicians that an alert awareness of the significance of this symptom as an indication for thorough colonic and rectal examinations would bring about many more earlier diagnoses than are now made. This alteration consists of constipation, diarrhea, alternating constipation and diarrhea, passage of blood or a change in the caliber of the stool. The presence of any one of these alterations in bowel function should make proctoscopic and sigmoidoscopic examinations, adequate rectal examinations and colonic investigation by contrast enemata obligatory.

Perhaps there has been nothing which has been more encouraging to everyone who is dealing with these lesions than the progressive increase in operability of these patients with carcinoma of the large bowel, as they present themselves for examination in the later years. Up to three years ago, our operability in terms of radical removal of the lesion was 69 per cent. Up to one year ago this had increased to 72 per cent, and during the last year the operability increased to 88 per cent. When 88 per cent of the patients presenting themselves for the question of surgery can be submitted to radical procedures, some explanation, of course, becomes necessary, and such a high operability rate cannot be expected in everyone's hands. This high rate is explained, we believe, (1) by the fact that many early carcinomata are discovered by the members of the gastro-enterologic and proctologic departments of the clinic while making routine examinations, (2) by the fact that many of the patients upon whom we operate are sent to us for operations because of our interest in this subject and so are within the operable stage, and finally (3) by the fact that with widening experiences with the operation many carcinomata of the colon and rectum are removed even when moderate-sized metastatic nodules are present in the liver. The position that the radical

removal of the growth either in the colon or rectum should be undertaken, even in the presence of small metastases in the liver, has been quite universally accepted by all who are dealing with these cases in any considerable number. It is now quite generally accepted that the death from distant metastases is not only delayed by the removal of the local growth, but is much less distressing than that associated with the local extension of the growth left in place.

From the point of view of the percentage of cases in which various types of operations are performed, it will be of interest to state that 20 per cent are performed by the one-stage abdominosacral procedure, 65 per cent by the two-stage abdominosacral procedure which has been described, 11 per cent with the loop colostomy and a posterior resection, and 4 per cent by means of the anterior resection.

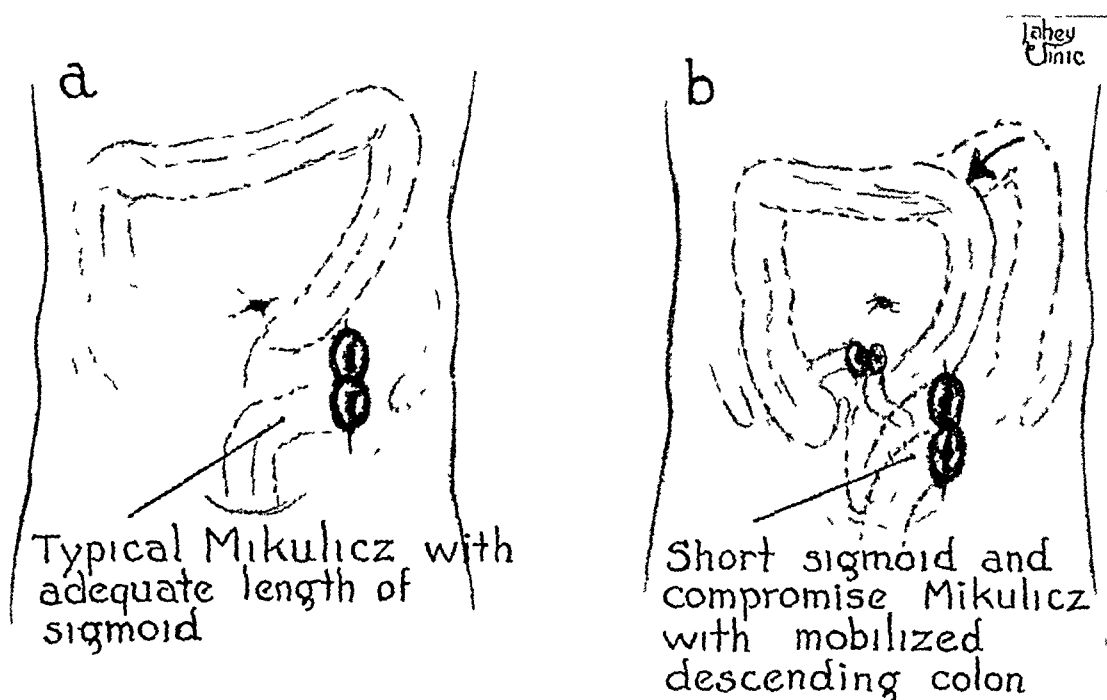


FIG. 3—Shows (a) the usual method of approximating the sigmoid loops in the typical Mikulicz procedure. This type of procedure is applicable when the lesion is sufficiently high in the sigmoid so that after its removal there is adequate length in the lower loop. (b) Shows the modification of the above typical plan when the lower loop of sigmoid is so short that it can hardly be brought up over Poupart's ligament.

Note that the splenic flexure has been mobilized and the upper loop of descending colon carried down into the pelvis and tacked onto the lower loop of sigmoid as it ascends straight out of the pelvis.

Note the sharp angle made in the mobilized descending colon where it is tacked to the lower sigmoid loop. Because of the danger of distention producing obstruction or tearing out of the approximation sutures here, note the addition of an ileostomy or cecostomy.

As the result of this experience, certain deductions have also been drawn relating to technical procedures. All colon resections in the clinic are performed with the modified Mikulicz plan of procedure. No resections with primary anastomosis are now being, or have for several years, been undertaken. It is unnecessary to mention the modification of the Mikulicz procedure with staggering of the proximal ileum which I have previously described, and it is also unnecessary to describe the type of two-stage abdominosacral removal of cancer of the rectum which I have also reported. It will be of interest, however, to mention a few of the technical procedures

which we have developed as a result of this experience, to meet certain conditions which arise in connection with the radical removal of carcinoma of the colon and rectum

Figure 3 shows a method of restoring the fecal stream by the modified Mikulicz plan of procedure when the carcinoma of the colon is too high for an abdominosacral removal of the rectum but too low for the typical Mikulicz type of procedure. As will be seen in the illustration, if the loop of sigmoid is sufficient in length to be brought straight up from the pelvis to the level of the skin, a long loop of descending colon may be obtained by mobilizing

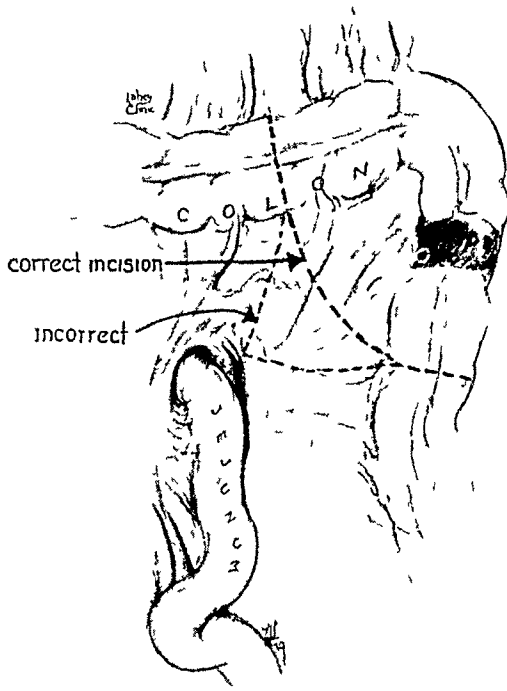


FIG. 4—Shows the proper and improper method of removing the mesentery in resections of malignancies in the splenic flexure. Note in the improper plan, the mesentery has been taken off close to the root of the jejunum. At this level the mesentery is delicate and tears easily when sutures are introduced. When the dissection is carried out this close to the jejunum the defect in the mesentery cannot be safely approximated. Until we learned to leave this apron of mesentery about the jejunal angle we had difficulty with sutures here and lost patients, loops of small intestines strangulating in defects here due to the sutures in the mesentery pulling out as a result of vomiting. When an apron of mesentery remains the danger of rupturing the mesentery at this point with an angulated loop of small intestine through this defect does not occur.

the splenic flexure, so that the lower end of the descending colon can be placed in the pelvis beside the pelvic loop of sigmoid. These two loops are tacked together as shown in Figure 3b, so that when the spur between them is crushed later there will be a direct descent of feces into the rectum. These procedures have now been employed in the clinic for a number of years and have saved several patients from being otherwise forced to have a permanent colostomy. One should not fail to realize, as we have had sadly impressed upon us by such an experience, that when the loop of colon is so angulated in the pelvis, as is shown in Figure 3b, that it can be placed beside the straight loop of distal sigmoid, there will be an angulation at the lowest point of the proximal colon. Should distention occur, not only will obstruction result at this point but there will be marked traction upon the stitches which attach this portion of the colon to the distal colon. Failure to appreciate this fact undoubtedly caused us one fatality. One should not fail in such cases to establish a cecostomy or ileostomy, thus taking the distention

and traction off the angulated colon and its approximation suture line. When the septum between the two segments of colon has been crushed and the fecal stream established, the ileostomy or cecostomy may then be closed.

Figure 5 shows a method of delayed restoration of the fecal stream when anterior resection is employed for a carcinoma of the sigmoid too high for abdominosacral removal and too low for the employment of the modified

Mikulicz type of resection In three cases we have cut off the sigmoid just above the reflection of the pelvic peritoneum, turned the ends in carefully with buried sutures, dropped this end into the pelvis and resected that portion of the sigmoid above this, containing the malignancy, and established a colostomy in the left side At the end of three to five years if no recurrence has taken place, the plan shown in Figure 5c is employed to restore the fecal stream A preliminary Mikulicz type of ileostomy is first performed, pulling out two loops of ileum close to the ileocecal valve, attaching them together after the Mikulicz principle The ileum, at the end of three or four days, is then opened and the entire fecal stream thus side-tracked Irrigation through the distal ileum is then carried on, until all of the colon is entirely defunctionalized When the colon has been thoroughly cleansed and when it contains no feces, the colostomy shown in Figure 5b is then dissected free from the abdominal wall through a left rectus incision, and the splenic flexure so mobilized that the proximal end of the descending colon can be approximated

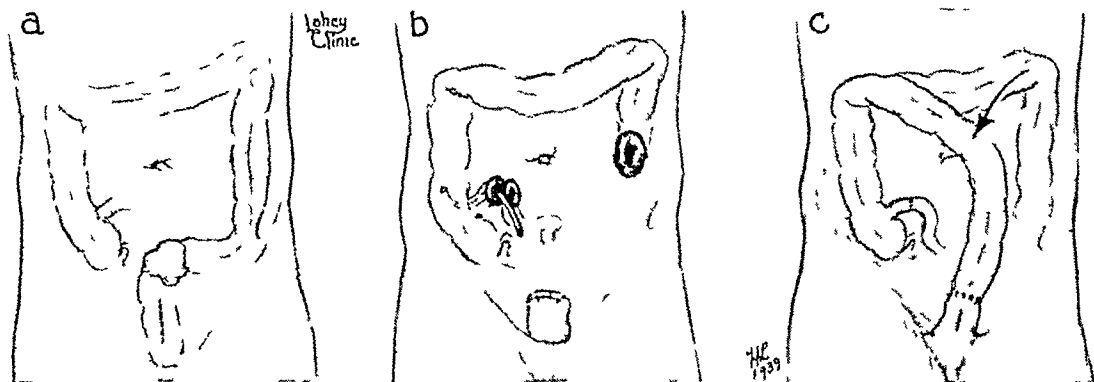


FIG 5—Demonstrates a method of restoring the fecal stream in low sigmoid malignancies, three to five years after anterior resections. A Mikulicz type of ileostomy is performed close to the ileocecal valve. The feces are entirely sidetracked from the colon beyond this point and defunctionalized by irrigation. The small remaining segment of rectum, after the anterior resection (b) is cleansed by enema, and when the colon distal to the ileostomy is clean, the colostomy is excised, the splenic flexure mobilized and the proximal end of descending colon approximated to the stump of the rectum intraperitoneally. The upper closed end of rectum is cut across and an accurate end to end anastomosis performed.

to the stump of rectum which has been left in the pelvis. The upper closed end of the rectum is then cut across and a direct end-to-end anastomosis, with careful mucosal and muscularis sutures, can be performed safely on a bowel which does not contain feces and through which no feces will be permitted to pass until sound union between the two ends has taken place.

At the end of two weeks, when sound union has taken place, the spout in the Mikulicz ileostomy is then crushed and the fecal stream thus reestablished through the large bowel. As soon as good bowel function is demonstrated by the passage of feces and by means of a roentgenogram after a barium enema (Fig 6), the Mikulicz ileostomy is then closed extraperitoneally. This procedure is useful, in that one can perform a radical operation upon these patients, can give them from three to five years in which to demonstrate whether or not recurrence is to take place, and at the time when the abdomen is opened for the reestablishment of the fecal stream it can be demonstrated whether or not recurrences are present. This, it has seemed to

us, is a useful and justifiable procedure in certain cases for delayed restoration of the fecal stream. It has also seemed to us a much simpler and effective defunctionalizing procedure than that proposed by Devine.

A small but useful technical procedure in patients with the colostomies associated with abdominocolic removal of the rectum and also those associated with the Mikulicz procedure is shown in Figure 7. While one can, with reasonable safety, remove the closure clamps on colostomies at the end



FIG 6—Roentgenogram following a barium enema showing the restoration of the fecal stream. X—site of anastomosis.

of 12 to 24 hours, it is desirable, when feasible, to give these wounds about colostomies as much time as possible in which to seal themselves off. Not infrequently the chief cause of complaint in patients with colostomies having clamps still on the implanted ends of their colons is the accumulation of gas, and in such patients, the introduction of a catheter into the ballooned colostomy by means of the purse string suture has proven useful and has permitted delay in the removal of the clamp (Fig 7).

Perhaps there is nothing which has done more to hold back progress in operations upon patients, particularly with carcinoma of the rectum, than the question of permanent colostomy. It is unfortunate that the colostomy with which most patients, and most family physicians, are familiar is the

colostomy for inoperable carcinoma. It is unfortunate that both patients and family physicians are not more familiar with the infinitely more satisfactory colostomies which are established when the lesion is removable and has been taken out by a radical procedure. No one can compare a situation of a colostomy in a patient with an inoperable lesion with the colostomy in a patient whose lesion has been removed. In the colostomies for inoperable carcinoma it is impossible to adequately control the bowel function. Many of the symptoms of which the patient with nonremovable carcinoma complains are not associated at all with the colostomies but rather with the inoperable lesion. It is because of these facts that many of the prejudices against permanent colostomy exist.

There are certain points concerning colostomies which have been established in instances with removable malignant lesions of the colon and rectum which need stating.

First, there are no trick colostomies whereby one can offer a patient anything in the way of bowel control. Control of bowel function is entirely related to the ability of the patient to learn how to constipate himself by a proper diet. If one performs a colostomy and discharges the patient without keeping him under supervision, preferably by personal contact, until he has learned to manage his colostomy, one can be certain that that patient, in most instances, will have a colostomy which will be unsatisfactory. One must realize that a period of four to six months must elapse before a colostomy functions most satisfactorily, and before the patient learns to so manage his diet and his colonic irrigations that he controls his bowel function satisfactorily.

I have often said that there is no place where the value of continuing interest and advice is better evidenced in a successful outcome than in the immediate six-month period following the establishment of a colostomy. Not only is it essential that these patients with colostomies have someone to whom to turn for advice during the first six months after their colostomy is established, but they must also be taught to bring their colostomy problems immediately to their adviser's attention as soon as they arise. Unless this is possible they soon become discouraged and unhappy. These patients soon learn to modify their diet so that the bowel function can be adequately controlled and, with time, even to take certain liberties with their constipating diet.

There will be occasional colostomies in which in spite of the establishment

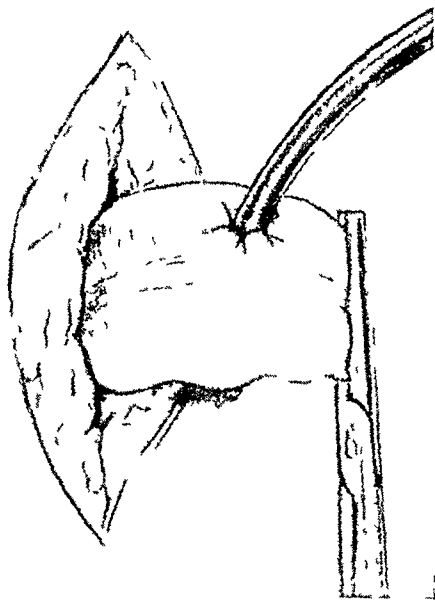


FIG 7—Shows the method of introducing a catheter in the gas filled colostomy with a retaining clamp still in place. By this procedure gas distention can be overcome and the removal of the clamp with wound soiling need not be done for some days.

of a good level of mucosa well above the level of the skin there will, at the end of some years, be a stricture in the skin about the colostomy opening. In such cases patients will frequently complain that they can introduce their irrigating enema but that its return is accomplished with great difficulty. In many of these patients if the examining finger be introduced into the stoma it will be found of such small caliber that the tip of the little finger will be barely admitted. In cases of this character a plastic skin and fascial operation by means of which a section of skin and fascia is removed about the colostomy opening, thus making a wide opening to the colostomy, will usually overcome this difficulty entirely. It is of interest to report, in view of the abhorrence with which colostomy is viewed by many patients and by many doctors, that of all the colostomies which we now have functioning after radical removal of the lesions, 75 per cent of the patients wear no bags whatever, employing only a piece of gauze over their colostomy, so confident are they of the control of their bowel function by constipating dietary regimens.

One should never discuss this subject, I believe, without mentioning mortality. When the operability, three years ago, was 69 per cent, our mortality was 13 per cent. With the operability now, during the past year, at 88 per cent, the mortality has fallen to 10 per cent. Mortality rates must always be kept within reasonable limits, but when one undertakes radical removal in borderline cases to offer patients the chance of the removal of the local growth, pride in operability rates should not be permitted to interfere with the prospect of possible relief with such hazardous procedures.

Just as mortality rates should always be reported, so we believe should end-results. These may be stated simply, as they have been repeatedly published from this clinic: 47 per cent of the patients with carcinoma of the colon who have had radical operation are alive and well over five years, without recurrence, and 42 per cent of the patients with carcinoma of the rectum who have had radical operation are alive and well over five years, without recurrence.

CONCLUSION

The relationship of polypi and adenomata to carcinoma of the rectum and colon is discussed.

The opportunity to attack the problem of carcinoma of the rectum and colon by the early discovery of the premalignant lesion and its removal by fulguration through the proctoscope or by colotomy is stressed.

The need for more routine proctologic and sigmoidoscopic examinations is evidenced by the number of polypi and adenomata which we have found and removed in the course of these routine examinations.

In 100 cases of carcinoma of the right colon, 100 cases of carcinoma of the left colon and 100 cases of carcinoma of the rectum, alteration in bowel function was noted in the history in 97.5 per cent of the cases.

The operability in the cases has risen in the last year to 88 per cent.

A few technical measures developed during the course of this experience are presented

The public (medical and lay) needs to be made aware that life with a colostomy in a patient cured of cancer is a much more satisfactory one than is life with a palliative colostomy for inoperable carcinoma. This is a most important and generally unrealized truth. Failure to realize the change that has taken place in the sequelae following colostomy is still holding people back from being cured of carcinoma of the rectum and colon.

The mortality is stated—10 per cent! The percentage of nonrecurrence at the end of five years is 47 per cent in patients with carcinoma of the colon and 42 per cent in patients with carcinoma of the rectum.

DISCUSSION—DR HARVEY B. STONE (Baltimore, Md.) Doctor Lahey said that the earlier the discovery and the smaller the rectal polyp, the more radical should be the treatment, because thereby the patient had a better chance for permanent cure. The specific problem on which I should like him to comment is whether, in the case of a small, apparently benign polyp lying in the rectum, he would follow so radical a procedure. I have not felt it was good judgment to subject such a patient to an extremely radical operation. I would like him to interpret just what he means by a radical attack on such lesions.

One more word—much as I respect his judgment and opinion, and bow to his wide experience, I cannot agree that the principle of a preliminary colostomy should be invariably and without exception applied to all diseases of the large bowel. Cases in which there is no obstruction can be safely handled in general by direct attack, and in many such cases a resection can be accomplished successfully. I question whether one should adopt an invariable principle of making a two- or three-stage procedure as a rule, when there are a number of cases which experience has shown may be safely handled by direct resection at the first session.

DR FRED W. RANKIN (Lexington, Ky.) I, of course, subscribe heartily to the thesis that the development of malignancy upon a benign polyp is a well established principle. A number of years ago FitzGibbon and I followed 13 cases of cancer of the colon and rectum through the various stages from benignancy to malignancy, confirming the work of Westheus and others, and establishing to our own satisfaction the proof that such a process takes place in a high percentage of cancers of the lower gastro-intestinal tract. Another important point, I think, in the support of this thesis, is the high number of cancers occurring in the sigmoid and rectum in the exact region where polypi are most frequently found.

In discussing types of operations and the applicability of radical surgery to low grade malignancy, I probably misunderstood Doctor Lahey in feeling that he said radical surgery should be applied to precancerous lesions. I should like to ask him, however, if he has changed his attitude toward the desirability of the one-stage operation. If I heard him correctly, his figures showed that only 20 per cent of the cancers of the rectum were operated upon by the one-stage procedure, while the two-stage operation was employed in the vast majority of cases. In 1929, I devised a two-stage radical operation for cancer of the rectum modifying Miles' procedure. In this operation a colostomy was made in the groin, the lower end of the bowel turned in and dropped back into the abdomen. One year later, Doctor Lahey modified

this procedure, bringing out the lower end of the bowel above the pubis and using it to irrigate through-and-through. I have not employed his procedure because I have hesitated to divide an obstructed bowel, and if the bowel is not obstructed more than moderately its decompression can be accomplished equally as satisfactorily by irrigations per rectum.

Having performed my own operation in a large number of cases with a satisfactory mortality, I turned four years ago to the Miles operation to replace it, and since then I have performed 87 one-stage Miles operations, six of my own operations, and 25 posterior resections and colostomy by Mumme's method. In this group of Miles operations the mortality has been 6.5 per cent, and I am confident that there is small utility for the two-stage procedure in the vast majority of instances. With adequate bowel decompression and rehabilitation I believe the one-stage operation can be accomplished with a mortality about equal to the two-stage radical procedure, and certainly it is a more desirable operation.

I trust Doctor Lahey will forgive me if I substitute "exteriorization" for the term "Mikulicz operation" as he uses it. Exteriorization was first done by Bloch, of Copenhagen, in 1892, and later in the same year by Paul of Liverpool. The latter resected the bowel and put a tube in the proximal loop for drainage. Mikulicz, in 1900, reported a large number of cases successfully operated upon by this method but gave full credit to these men for the establishment of the principle which reduced the colon mortality from around 40 per cent to 20 per cent, and has in consequence had the operation called after him here in America only. I certainly think it should be called an exteriorization or the Bloch-Paul-Mikulicz operation if you will. It is a useful procedure but only for very definite indications.

It seems obvious that the increasingly satisfactory results following surgery for cancer of the large bowel and rectum such as Doctor Lahey reports depend upon a number of factors, not the least important of which are adequate preliminary preparatory treatment, and utilization of multiple procedures either in one or more stages.

DR FRANK H LAHEY (Boston, Mass., in closing). In answer to Doctors Rankin and Stone: I am sure it is my fault that I did not make our position clearer. I did not mean to imply that we ever perform a radical operation for a benign lesion. We have performed local operations with malignancies in the tip of the polyp not involving the base and they have not recurred. With a frank carcinoma involving the mucosa and spreading to the base even if only the size of the little finger nail, we do radical operations. That is the point where the family physician and the patient plead for local operation, with which we have seen recurrences in six months to everybody's regret. Neither did I wish to imply that everyone should employ the Mikulicz procedure. The original procedure was nothing like the one to-day. It was justly criticized in its original form because of the local implantation of carcinoma in the wound with this plan of operating. With the Mikulicz operation which we and others have modified this objection is overcome and just as radical removals may be accomplished as with any other operation. Therefore, I see no reason why anyone who likes it should not employ it. Its employment is a matter of personal selection.

As to Doctor Rankin's question: are we modifying our operative procedures? Yes. We are doing more and more one-stage operations. Just as he began with the two-stage procedure, so should we all, and as we become more familiar with the technic we will become more willing to undertake a one-stage procedure. But if we had begun with a one-stage, our mortality would

have been unduly high. We have been slow in increasing our one-stage procedures, because we have had such good results in advanced cases, advanced ages and poor risks with the two-stage procedure, and because we have had such a high operability and reasonable mortality.

We have just been in a predicament with carcinoma high in the jejunum and what we did may prove useful to others. The carcinoma was close to the ligament of Treitz, and after an adequate resection of the jejunum there was not enough jejunal stump left to do a safe end-to-end anastomosis. Had it been brought down sufficiently to do an end-to-end anastomosis, it would have retracted beneath the mesenteric vessels and caused obstruction. We were faced with a difficult situation which was overcome in the following way. We cut the ligament of Treitz, took out the segment containing the tumor and turned in the ends. We then went over to the ascending colon, turned over the hepatic flexure, approached the retroperitoneal duodenum and found it could be mobilized. We then pushed the end of jejunum beneath the mesenteric vessels, with the result that we had a well mobilized retroperitoneal duodenum with the mesentery of sufficient length to permit it to reach over in front of the transverse colon. The apron of omentum was then divided up to the transverse colon, the lower segment of jejunum brought up in front of the transverse colon as was the upper segment of duodenum, and a lateral antecolic anastomosis established between them.

I have been faced with this difficulty in cases of gastrojejunal ulcer. When there is a short jejunal stump it is often difficult to make a satisfactory end-to-end anastomosis. I am sure that mobilizing the retroperitoneal duodenum will give a very satisfactory lateral antecolic anastomosis or end-to-end anastomosis which will function well and much better than a difficult end-to-end anastomosis high up in the jejunal fossa.

TECHNIC AND DEMONSTRABLE ADVANTAGES OF THE DEVINE COLOSTOMY*

REGINALD H. JACKSON, M.D.
MADISON, WIS.

I APOLOGIZE to those members of the Society whose wide experience in surgery of the colon warrants their designation as masters in this field. Doubtless they are already familiar, and have had far more experience, with the Devine colostomy than I. The decision to present our limited experience at this meeting was activated by two reasons: first, conversations with colleagues in the West revealed that many of them either missed Devine's communications in the literature or were not favorably impressed with his contribution. Possibly the nonavailability of the special enterotome essential to the proper execution of one of the steps has militated against more general adoption of the method. Second, we are thoroughly convinced that the Devine colostomy is a distinct improvement over the usual spui type, and confers so many benefits not only upon the patient but also upon the general surgeon that he cannot afford to overlook it.

During the past 30 years, I have, as a general surgeon, many times run the gamut from enthusiastic enterprise to dull despair as regards resection of the distal colon for malignant neoplasms, finally becoming resigned to the attitude of accepting such cases as a duty, but doing so without that concomitant sense of probable victory which is such a sustaining power in all surgical endeavor.

Our recent experience with the Devine procedure has renewed our interest in this field. We are convinced that faithful adherence to Devine's admonition not to resect the diseased bowel unless, and until, the distal colon is completely defunctioned and thoroughly decontaminated will remain an enduring cardinal principle in this field. While the goal attained by Devine of reducing the mortality rate of his colon surgery to one which bears comparison with the mortality rate of his other operations in the abdomen must remain a utopian dream for the general surgeon, there remains ample opportunity for him to contribute greatly in reducing the deplorably high general mortality rate.

While the outstanding results of recent years achieved by Rankin, Lahey, Dixon, and their confieres in this field are notable for a decided lowering of personal mortality rates, we must frankly face the fact that the huge majority of these patients are cared for by the general surgeon.

Any method which will insure a lower general mortality rate must be *per se* of such a nature that it is generally applicable and not directly dependent

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 6, 7, 8, 1938.

THE DEVINE COLOSTOMY

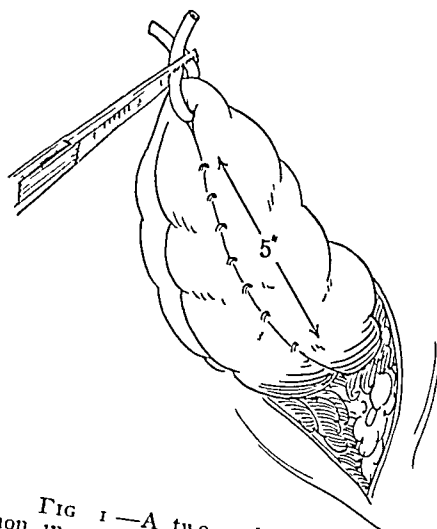


FIG 1—A two and one half inch incision in upper right rectus. Loop of transverse colon withdrawn and supported on rubber tube adjacent white lines tracked together for five inches. Loop replaced until upper tracking suture is at level of peritoneum. Mesocolon above tracking suture has been doubly ligated and divided to permit swinging of mesentery into new lateral position.

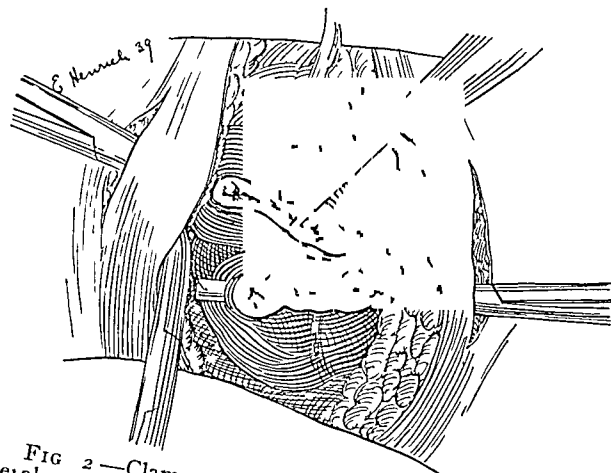


FIG 2—Clamps have been inserted through small lateral incisions at midwound level, grasping top of colon loop. Division and sterilization with diathermy current. Lateral incisions go through skin and fat only (not through muscles).

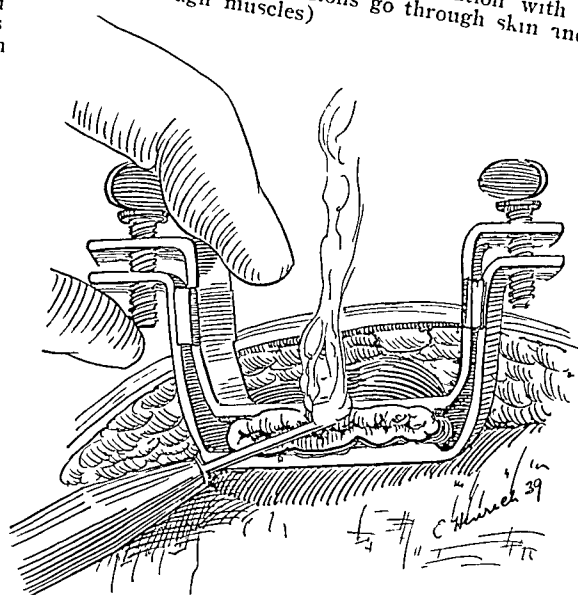


FIG 2A—Special Devine colon closing traction clamp in place. Sterilization with diathermy current.



FIG 3—After withdrawal of clamps with bowel ends peritoneum is closed rather snugly, wound scrubbed with soap and water and closed by layer method. Devine advocates tracking peritoneum to bowel. We have not found this necessary.

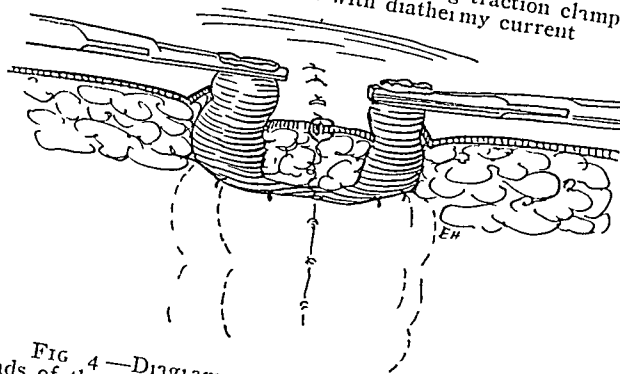


FIG 4—Diagrammatic section to show the two cut ends of the bowel drawn up through the small openings by Kocher clamps, and the main wound sutured.

upon the acquisition by the general surgeon of such excellent skill and technique as to approach the perfection of the masters

The slowly improving general results achieved in the past 25 years must be credited to the acceptance by the general surgeon of the multiple-stage procedure. Where the element of obstruction is present, the establishment of a decompressing colostomy is a *sine qua non* of success in the resection stage.

No doubt these are elementary observations. Everyone knows how to make a colostomy, but only after experience with the Devine colostomy can one properly estimate the demerits of the usual spui colostomy.

As the technique and demonstrable advantages of the Devine colostomy can be far better portrayed in pictures than by words, I shall resort to the film

TECHNIC OF THE DEVINE COLOSTOMY TO "DIFUNCTION" THE COLON

A vertical incision two and one-half inches long is made in upper right rectus

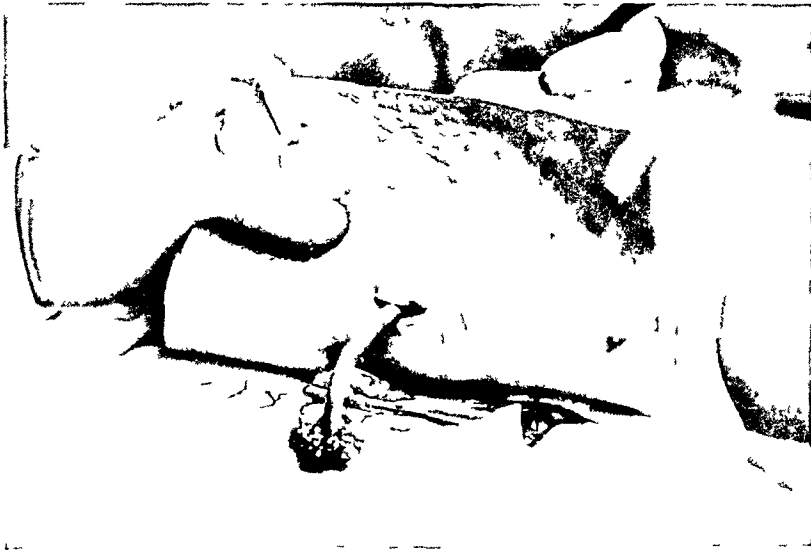


FIG 5—When an acutely emergent obstructive condition is present decompression of proximal loop is secured by passing a large catheter into the proximal rectus and threading a rubber sponge pad over it

The glove on the left hand is vaselined to facilitate the abdominal survey. The transverse colon is withdrawn and suspended by a rubber tube (Fig 1).

The adjacent "white lines" are tacked together for fully five inches (Fig 1).

The peritoneum is tacked to the bowel at the upper level of above row.

Knife punctures are made (skin and fat—not through muscles) one inch from the skin edges at midwound.

Clamps through punctures grasp the tip of the bowel loop (Fig 2).

The loop is divided and sterilized with the diathermy knife (Fig 2).

The bowel clamps are withdrawn and placed on the abdominal wall (Figs 3 and 4).

The wound is thoroughly scrubbed with soap and water.

The incision is closed, first the rectus muscle and sheath above and below

the colon and then the skin, and the proximal meatus is then tacked to the skin

A thick benzoin protective dressing is placed over the incision, leaving both meati exposed

If the obstruction is emergent, as shown roentgenologically, the proximal clamp is removed and the proximal loop of the bowel decompressed at once

If the transverse colon is greatly distended, Devine advises performing a simple cecostomy and a few days later performing the colostomy

In the average case, the proximal clamp is removed after 48 hours and a suitable tube introduced through a soft rubber sponge pad (Fig 5)

The proximal bowel is flushed out thoroughly each morning

The tubes are corked between washings (Figs 6 and 7)

Patients are encouraged to be up and walk around at the end of a week

The distal clamp is removed in three days and irrigation started. Instillation of petrolagar helps to soften and remove fecal lumps. We have also found that a continuous tap water drip into the distal loop during the night helps in breaking down hard fecal accumulations

Male patients irrigate themselves in the toilet for a half hour, twice daily. Women prefer the assistance of a nurse who inserts a small anoscope which empties into a bedpan. Elevating bed facilitates flow

A shrunken, defunctioned bowel facilitates mobilization and resection amazingly. In two instances the preliminary survey noted that on account of the extensive growth and its "frozen" condition, it was questionable whether a resection could be accomplished later. In the most dubious case, an additional (third) week of colon flushing was instituted. The night before the day set for resection, the patient developed an acute intestinal obstruction with fecal vomiting. Operation revealed that the obstruction was due to an old appendiceal adhesion band in the right lower quadrant. It was noted on the record that the extensive, immovable "frozen mass," noted in the original survey, had been reduced fully 50 per cent and the sigmoid was somewhat



FIG 6—A simple method of flushing out the proximal loop every morning

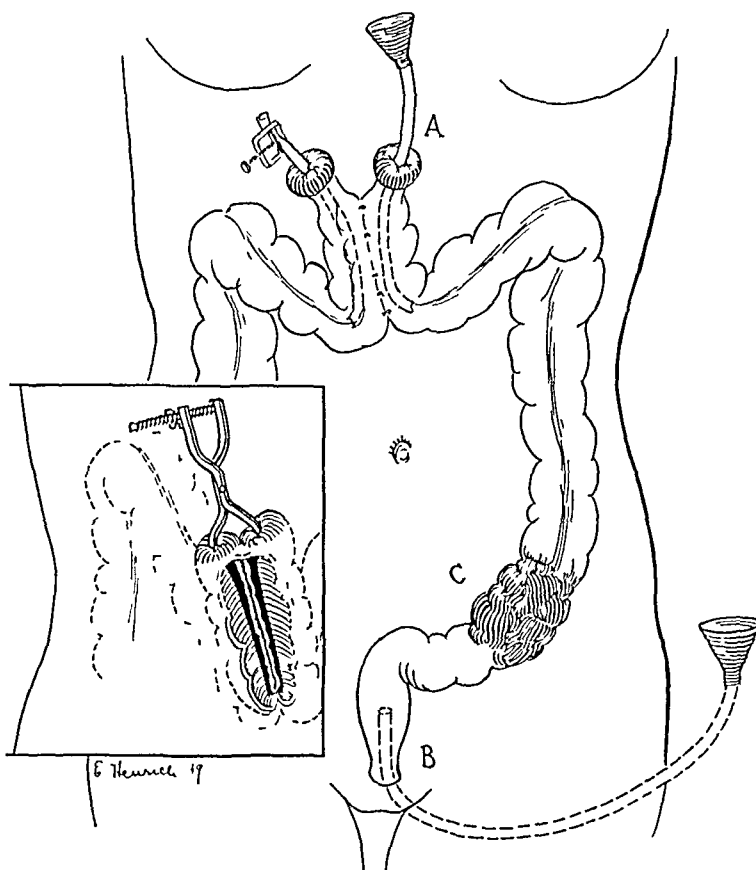


FIG 7—Double barreled colostomy. Distal colon completely de-functioned flushed out twice daily. Proximal loop flushed once daily. Tube clamped off between flushings to prevent dehydration.

Insert Special Devine instrument to be applied to restore continuity of colon after resection stage.

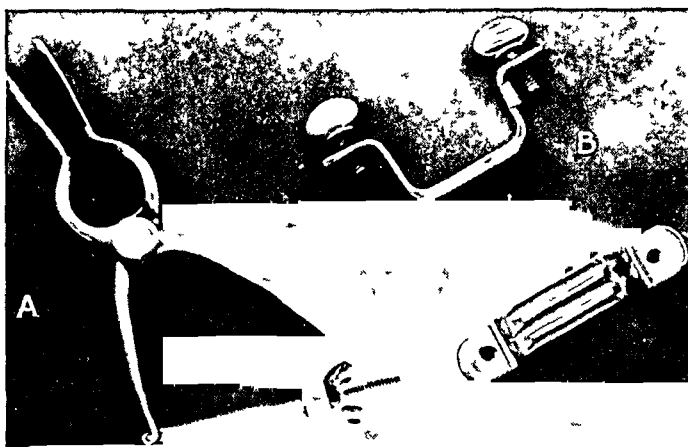


FIG 8—Crude homemade Devine special instruments. A Enterotome to crush partition and restore colonic current after resection stage. B Occlusion clamp used in resection stage. To be placed on proximal end of distal sigmoidal segment.*

* These instruments are now made by the V. Mueller Company, Chicago, Ill.

movable Twelve days later, the resection proved to be very feasible Since this experience we wait a month before performing the resection, believing that the gain thus secured outweighs any conceivable extension of the neoplastic growth itself Patients with a continent proximal meatus are perfectly willing to wait, as they are up and around

The left ureter and arteries are identified with the Cameron light We always have a left ureteral catheter *in situ*

The Devine special intestinal occlusion clamp we have found most satisfactory This and the Devine enterotome are crude, homemade ones, as there were no special Devine instruments on the American market (Fig 8)

A low anastomosis is made, extraperitonealized with flaps, and a drain placed We believe, with Devine, that the surgeon will be encouraged with this method to attempt a lower anastomosis and thus save the sphincter, instead of performing a permanent colostomy and a Kraske You will note the ideally clean aspect of the opened specimens (Fig 12)

One is apt to make the small incisions for the meatus too large at first, but we have found that injecting quinine and urea shrinks the protruding mucous membrane around the tube in the proximal meatus

Ten days, or more, after the resection, the Devine enterotome is applied (Fig 9) and tightened each day, usually it works loose on or after the fourth day Exceptionally a week is required

Before tightening, a roentgenogram verifies the position of the blades (Fig 10) As the "fully five inches" of suturing the white lines together may easily be followed by a shrinking to less than three, we were fearful that the blades of the enterotome might extend too far and possibly penetrate into the free peritoneal cavity We thought it best, in the case illustrated, to draw the clamp well up before screwing home the nut

The final step, which is undertaken after the clamp has worked loose, and the satisfactory condition of the new channel ascertained by passing a finger through the proximal meatus into and through the opening into the distal loop,



FIG 9—Application of Devine enterotome Well vaselined blades introduced separately, then joined and screw clamp tightened each day Usually works loose in four to five days

is a very simple one. Under local anesthesia, the edges of the meat are mobilized, removing any indurated skin and mucous membrane inverting the mucosal layer and closing the skin except for an iodoform wick.

End-Result—Note restored continuity of colon (Fig 11). Devine states that he usually begins injecting fluid into the lower bowel per rectum a few days after the resection, and expects that if any fluid appears in the resection wound, a fecal fistula will result. This happened in about 25 per cent of his cases.



FIG 10—As a safety check, we introduce some barium in each meatus and before screwing the blades tight have a film made. If blades seem to project too far (possibly beyond the tacked-together area), it is corrected by drawing up instruments snugly before closing it.

In one of our cases, such a serious infection occurred in the resection wound that we felt sure the anastomosis would be utterly destroyed. We refrained from applying the enterotome for six weeks, until the wound had healed thoroughly and was completely epithelialized. When the continuity of the bowel was restored, the anastomosis worked perfectly. We believe, therefore, that it is wise not to test it soon after the resection but to delay it, especially if there is any infection in the resection wound.

Figure 13 shows a wound healed *per primam*, and the Devine enterotome was used on the tenth post-operative day. Figure 14 shows the

wound of a patient which became infected, as evidenced by the extensive scar formation, but who had an excellent end-result.

What, then, are some of the advantages of the Devine colostomy? They may be briefly enumerated under two headings:

I. *Benefits Conferred Upon the Patient*

Improvement in the patient's general condition before resection is far more pronounced because

- (1) Fluid equilibrium is better maintained. Control over the proximal meatus obviates the dehydration effect often associated with the spui type.
- (2) Morale is maintained at a much higher level in the absence of the more or less constant or unexpected escape of noisome gas and messy stool.
- (3) At the end of a week, they may be up and around, dressed and visiting friends and other patients without embarrassment.



FIG 11 --Roentgenogram after barium enema in case shown in Fig 13 in which an infected wound delayed restoration of colonic flow six weeks. Arrow points to gap in mucosa where a fecal fistula would have occurred. Two months later, this gap had closed up.

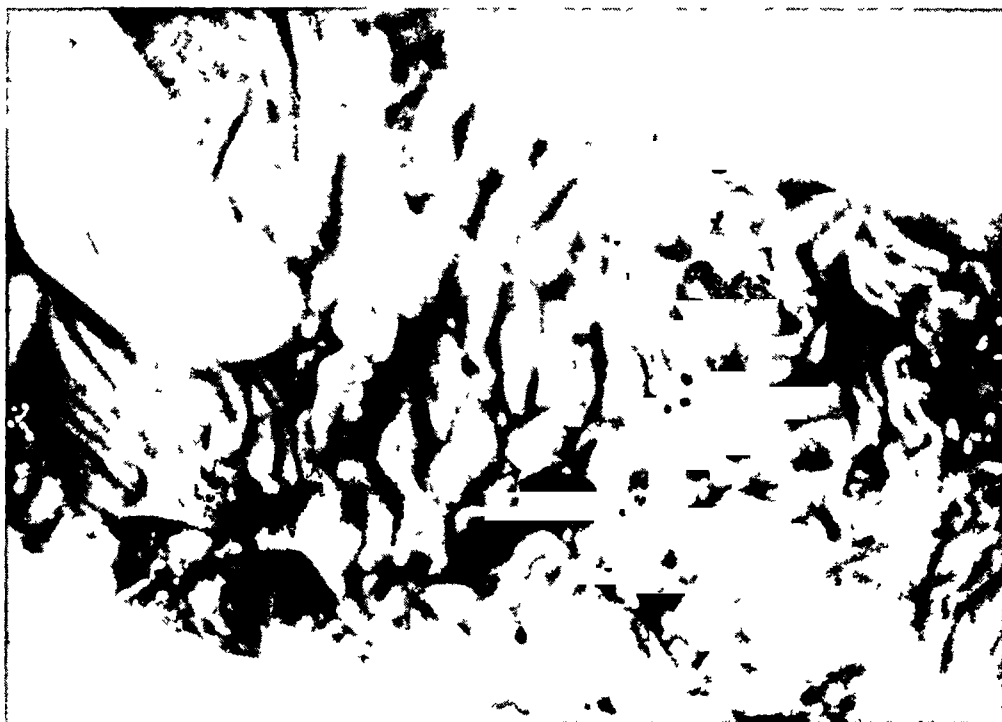


FIG 12 --Resected bowel, opened immediately after removal, shows clean, soft condition of bowel wall.

- (4) Intelligent patients may go home at the end of ten days and return for the resection stage after two weeks' colon washing at home
- (5) Another economic benefit results in that they may occupy a bed in a ward instead of being relegated to a private room
- (6) A patient thus prepared presents an amazing contrast in optimism, confidence, and constitutional fortitude as compared with one prepared by a spui colostomy with its attendant mental and physical depression

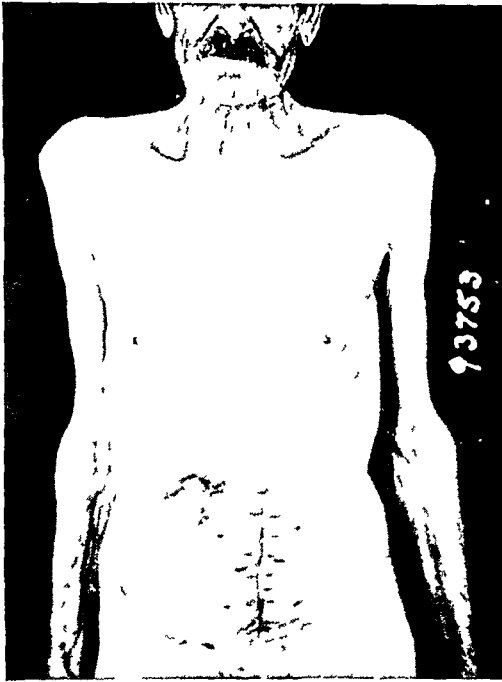


FIG 13—When the resection wound has healed without infection the restoration of the colonic current is made with the Devine enterotome a week or 10 days later

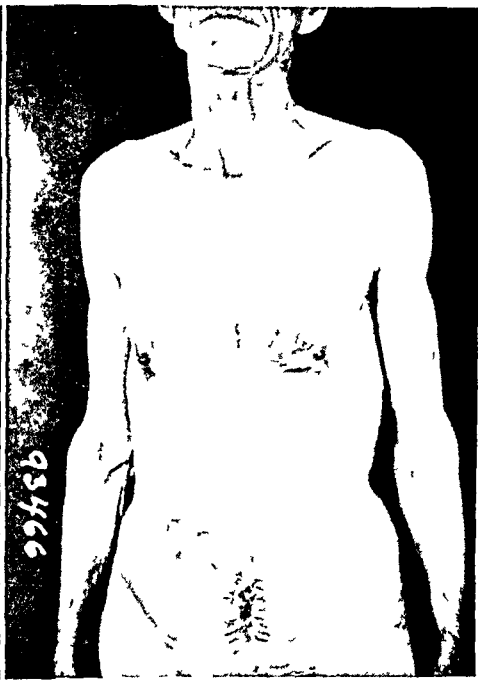


FIG 14—When the resection wound is infected and there is a strong likelihood of a fecal fistula forming, use of the enterotome is delayed until the wound has granulated in and is well epithelialized. In this instance, six weeks intervened

- (7) It confers a benefit on relations and friends in that it greatly reduces the horror of the treatment

II *Benefits Conferred Upon the Surgeon*

- (1) The distal colon, being completely detached and defunctioned, may, through repeated washings, be decontaminated more efficiently than in the spui type which, as noted by C H Mayo,² permits recontamination by the fecal stream splashing over and entering the distal loop
- (2) The position of the colostomy in the upper right quadrant insures a clean resection field with ability to mobilize the descending colon even to the splenic flexure at the resection and anastomosis stage
- (3) The completely clean and comparatively sterile condition of the

distal bowel encourages the attempt to resect and anastomose at a lower level and preserve a continent condition

Devine, in speaking of such a prepared bowel, says "I mean one which has been allowed to remain functionless until such time as the bacterial content has been considerably reduced, on the principle that if, experimentally, a segment of bowel be completely isolated and thus deprived of its function, in the process of time it will lose most of its bacterial content"

The victim of a spui colostomy is generally importunate in respect to time and begins very early to plead for the next stage operation. The patient with a Devine colostomy, being up and around, is very cooperative and quite content to wait the essential three or four weeks

- (4) If the resection wound develops infection and must be drained, a delay before applying the enterotome, of such time as it takes for the granulating wound to heal solidly, does not greatly discommode the patient and greatly diminishes the chance of fistula formation
- (5) The final closure of the colostomy mouths under local anesthesia is a minor procedure compared with the usual closure of a spui colostomy
- (6) In certain advanced, questionable resectable cases, it has, in Devine's experience, provided a comfortable probationary period, in that after the excision the rectal end is closed and peritonealized, the proximal sigmoidal end is implanted in the anterior abdominal wall, and the patient carries on comfortably with his established colostomy until the passage of time (six months to a year) reveals whether or not metastases have developed. If not, and if the patient's general condition warrants it, the sigmoidal end may be mobilized and telescoped into the revascularized rectal stump with good prospect of success

While our experience with the Devine colostomy has been limited, it has been most satisfactory

SUMMARY—The author, after briefly alluding to the general gloomy experiences of the average general surgeon over the past 25 years in the field of colonic surgery, acclaims, after recent personal experience, the many merits of the "defunctioned" colon as devised by Devine, and expresses the belief that while the general surgeon cannot expect, through the acquisition of the skill of the masters, to parallel their results, he will, by the adoption of the procedure, make a definite contribution in lowering the present too high general mortality rate. The technic, which does not require exceptional skill, is detailed and illustrated with pictures

CONCLUSIONS

The ever pressing problem of how to appreciably lower the general mortality rate in operations involving the resection of the distal colon for malignancy

nant neoplasms presents one hopeful aspect, in that it is more and more apparent that there is a direct relationship between the very high mortality rate of the average general surgeon in this field and the relative perfection or thoroughness of the pre-resection conditioning process. While the usual type of spui colostomy has been of material service in the past, the development of the "continent" proximal colostomy meatus by Devine confers so many benefits upon both the patient and the surgeon that its general adoption should be accompanied by a decided lowering of the high general mortality rate. Devine⁵ estimates this to be 30 per cent in Australia.

REFERENCES

- ¹ Devine, H. B. Safer Colon Surgery. *Lancet*, March 21, 1931.
- ² Mayo, C. H., and Dixon, C. F. A New Type of Permanent Colostomy. *ANNALS OF SURGERY*, 87, 711, May, 1928.
- ³ Devine, H. B. Carcinoma of the Colon. *Brit. Med. Jour.*, 2, 1245, December 28, 1935.
- ⁴ Devine, Sir Hugh. Operation on a Defunctioned Distal Colon. *Surgery*, February, 1938.
- ⁵ Devine, Sir Hugh. Personal communication.

DISCUSSION—DR ALTON OCHSNER (New Orleans, La.) One of the difficulties that has occurred to us has been the fact that a certain portion of the bowel is sacrificed in putting on two clamps and putting them through the lateral incision. If one will turn the loop of bowel through an arc of 90°, the loop lies longitudinally and one can place the clamps close together. A better method is a transverse incision rather than a longitudinal one, bringing the two loops out each end of the incision without contaminating the subcutaneous tissue.

The clamp we have used is a modification devised in our clinic, which is much simpler than the Devine clamp, it is made of aluminum and is very light. It can be tightened, there is a guide telling the degree of separation of the clamp. We have had 16 patients upon whom we have performed the Devine colostomy, seven for carcinoma and nine for infection. There have been seven with the first stage and nine in which the second stage was completed. One of the first-stage patients died of pneumonia several weeks after the operation.

I want to subscribe to this operation, because "defunctioning" of the bowel makes resection on the left side much safer.

DR REGINALD H JACKSON (Madison, Wis., in closing) One of my chief reasons for presenting this subject was to popularize the Devine type of colostomy among the general surgeons, many of whom are forced to perform an emergency colostomy for acute intestinal obstruction due to a malignant lesion in the colon, but do not feel capable of performing a later resection, referring such cases to colon resection specialists.

The Devine colostomy, in its performance, does not require any special skill. Patients thus treated will come for resection not only in far better general condition, but also with the resection area in ideal condition through "debacterIALIZATION" to better insure a successful outcome.

THE EFFECT OF ACUTE INTESTINAL OBSTRUCTION ON THE BLOOD AND PLASMA VOLUMES

SAMUEL GENDEL, M D , AND JACOB FINE, M D

BOSTON, MASS

FROM THE SURGICAL RESEARCH LABORATORY, BETH ISRAEL HOSPITAL, AND THE DEPARTMENT OF SURGERY, HARVARD MEDICAL SCHOOL, BOSTON, MASS

FROM A GROUP of studies on intestinal obstruction already completed,^{1 2 3 4} and from experiments still in progress, we have made the following observations (1) Ligation of the cardia and ileocecal valve (*i e*, closed-loop obstruction of the entire stomach and small intestine) in the cat, the gastro-intestinal tract of which has been rendered free of food, fluid and gas by a preliminary 24-hour period of starvation, does not cause notable disturbances in the gastro-intestinal tract. Death results in a few days primarily because of dehydration and starvation. (2) The introduction of various types of food into such closed loops, depending on the kind of food used, may result either in rapid death from the accumulation of gas and fluid under great tension or slow death with only moderate or insignificant quantities of gas and fluid. (3) The survival time of cats dying from gaseous distention is inversely proportional to the intra-intestinal pressure. (4) The inhalation of 100 per cent oxygen will reduce the intra-intestinal pressure in gaseous (nitrogen) distention to normal, or nearly normal, and substantially prolong the life of the animal. (5) Gaseous distention, at or above the pressure levels observed in obstruction in man and animals, does not notably increase the volume of intra-intestinal fluid, the weight of the bowel wall, or the fluid in the peritoneal cavity above the normal. (6) Dehydration alone does not account for the rapid death of such animals. (7) Denervation of the extrinsic nerve supply to the intestine does not influence the survival time of these animals. (8) We have further observed that high grade intestinal distention increases the femoral venous pressure without affecting the jugular venous pressure. Studies now in progress by the plethysmograph and by assays of water content of muscle tissue of the lower extremities suggest that distention may, by compression of the abdominal vessels, cause a loss of plasma into the tissues distal to the site of compression.

We present in this communication a study of the effects of distention, at levels of pressure observed clinically, on the volume of the plasma and on the total blood volume in dogs.

Method —The plasma volume of 18 dogs was determined by the method of Gibson and Evans,⁵ who used a blue dye (T-1824 or "Evans Blue"), the concentration of which in the blood was measured by the photo-electric microcolorimeter (Gibson and Evelyn⁶). This dye is nontoxic in the dosage used and very slowly diffusible. The error of other methods, arising from

variable degrees of mixing of dye with the blood, is eliminated by taking multiple blood samples at accurately known intervals. By extrapolating the disappearance slope of the dye from the blood to the time of injection of the dye, the plasma volume can be calculated with variations not exceeding 2 per cent in duplicate samples. Since 30 to 35 cc of blood are required for each determination, this volume was duly considered in the calculations. With the plasma volume known, the total blood volume was calculated from the measured plasma volume and hematocrit.

The normal values were determined in all but several large dogs a week before the day of experimental obstruction. In these exceptional instances this was done on the same day. All measurements were made under intraperitoneal nembutal anesthesia.

Four groups of dogs were studied (Table I). Two dogs comprise the first or control group. Nothing was done to them except to keep them under intraperitoneal nembutal anesthesia and to make plasma volume determinations every 24 hours until they died, one after 60 hours, the other after more than 72 hours. One of the two dogs (Dog 18), received 500 cc of 5 per cent glucose in physiologic saline each day following the plasma volume determination. Two dogs comprise the second group. They were prepared as follows. After 24 hours, during which time only water was allowed so that the small intestine would be empty and collapsed, intraperitoneal nembutal anesthesia was administered and an occluding ligature placed around the pylorus. The terminal ileum was divided, the distal end inverted, a cannula was inserted into the proximal end, brought out through a stab wound, clamped off, and the incision closed. Plasma volume determinations were made after four hours and again after 23 hours. Death occurred in one after 31 hours, in the other after 34 hours.

The third group included 11 dogs. They were prepared similarly to those of Group II except that after dividing the ileum and closing the distal end a cannula was inserted into the proximal end and connected, after being brought out through a stab wound, to a Perusse pressure bottle. The entire small intestine was then continuously inflated with air at a constant level of pressure. Fifteen cm of water pressure was used in six dogs, 20 in four others, and 30 in one. Plasma volume studies were made after four hours in nine dogs, after 13 hours in two and after 18 to 23 hours in five. The average survival time was 20.8 hours.

Three dogs treated in exactly the same manner as those in Group III, and subjected to pressure of 40, 30, and 20 cm of water respectively, died after 10, 12 and 18 hours, with an average survival time of 13 hours. Their more rapid death was due to the unanticipated finding at autopsy of extensive venous congestion, mucosal degeneration and extravasation of blood and plasma into the intestinal lumen, mesentery and peritoneal cavity. They are, therefore, classified as Group IV, *i.e.*, as dogs with obstruction, distention and strangulation. Their short survival time permitted plasma volume determinations only once, after four to four and one-half hours.

From this and previous investigations, we learned that the resistance of the dog's intestine to increased pressure is notoriously poorer than that of the cat. Strangulation almost never occurs in the cat even at pressure levels of 80 cm of water, whereas in five dogs, subjected to 40 cm of water pressure death occurred so quickly from strangulation and shock that no plasma volume determinations were possible.

The distention pressure levels used in the dogs of Groups III and IV are reasonably close to those found in various types of obstruction in man and in experimental obstruction (without artificial distention) in dogs.⁷

The dogs were kept under intraperitoneal nembutal anesthesia until death occurred. In previous studies no substantial difference had been observed in the survival time of two groups of cats similarly prepared, one under anesthesia, the other awake, subjected to the same levels of distention and pressure.

Results—Table I shows that the average normal plasma and whole blood volumes of the 18 dogs studied were 5.0 and 8.8 per cent of the body weight respectively and that the average normal plasma volume was 56.8 per cent of the whole blood volume. These results are reasonably close to those of Gibson, Keeley, and Pijoan⁸ and of Gasser, Erlanger, and Meek.⁹ The former, using the method of Gibson and Evans, found that the normal blood volume varied between 8.4 and 9.7 per cent of the body weight. The latter (by a method probably less accurate than that of Gibson and Evans) found the average blood volume in a large series of dogs to be 9.7 per cent of the body weight and the plasma volume 60 per cent of the whole blood volume.

Part of the changes in plasma volume in these various groups of dogs are presumably due to the dehydration and perhaps pooling of capillary filtrate, especially in the dependent tissues, owing to muscular inactivity. Almost none of the dogs in the entire series discharged urine or showed a distended bladder at autopsy, so that it is not necessary to attribute any substantial part of the plasma volume changes to loss of fluid in the urine.

In control Group I, the plasma volume after 24 hours decreased 22.4 per cent in the dog which received no fluid and 18.6 per cent in the one which did, the average being 20.5 per cent. The loss of plasma for the same period in the two dogs of Group II (obstruction without distention) was 8.8 and 20 per cent, respectively, averaging 14.4 per cent. In contrast to these figures, the average plasma loss in five dogs of Group III (obstruction with distention) after 18 to 23 hours was 55.0 per cent (Table II and Chart 1).

The significance of these figures becomes impressive when translated into terms of the percentage of body weight which these losses of plasma represent, viz., 0.85, 0.7, and 3.1, respectively, in the three groups (Table II and Chart 2). Johnson and Blalock¹⁰ caused death in dogs when blood plasma equivalent to 2.4 per cent of the body weight was removed in 0.5 per cent fractions every six hours. The conditions prevailing in our experiments are comparable to those of Johnson and Blalock, who obtained their results by the removal of whole blood and the immediate reinjection of the red cells.

TABLE I

COMPARATIVE CHANGES IN PLASMA, WHOLE BLOOD, AND RED CELL VOLUMES AND IN HEMATOCRIT IN FOUR GROUPS OF DOGS

No of Dog	Weight	Intra-intestinal Pressure, Cm Water	Hours After Beginning of Experiment	Reduction in Plasma Volume			Reduction in Total Blood Volume			Change in Red Cell Volume	Hematocrit	Change in Hematocrit	Plasma Volume			Total Blood Volume			Red Cell Volume	Survival Time In Hours
				Plasma Volume	In	Per Cent	Total Blood Volume	In	Per Cent				Plasma Volume	In	Per Cent of Body Weight					
GROUP I																				
INTACT DOGS UNDER ANESTHESIA (NO DISTENSION)																				
17	16 8	0	0	736	0	1,472	0	736	0	50	0	43	86	43	86	43	60			
			24	573	22 4	1,372	6 6	802	+ 8 2	58	-16	3 4	8 1	4 7	4 7					
18	15 5	0	0	533	27 5	1,269	13 1	736	0	58	+16	3 1	7 5	4 4	4 4					
			0	665	0	1,279	0	614	0	48	0	4 3	8 3	4 0	4 0					
			24	542	18 6	1,032	18 0	490	-20	48	0	3 5	6 7	3 2	3 2	72 +				
			72	533	19 0	919	28 0	386	-37	42	-12	3 4	5 9	2 5	2 5					
GROUP II																				
OBSTRUCTION WITHOUT DISTENSION																				
12	7 5	0	0	304	0	573	0	269	0	47	0	4 0	7 6	3 6	3 6	31				
			4	303	0	577	0	274	+ 1 0	48	+ 2	4 06	7 6	3 6	3 6					
			23	277	8 8	554	3 3	277	+ 2 9	41	-13	3 7	7 4	3 7	3 7					
13	8 9	0	0	408	0	816	0	408	0	50	0	4 6	9 2	4 6	4 6					
			4½	352	11 2	708	13 2	356	-10 2	50	0	3 9	8 0	4 1	4 1	34				
			23	326	20 0	633	22 4	307	-24 7	48 5	- 5	3 6	7 1	3 5	3 5					
GROUP III																				
OBSTRUCTION AND DISTENSION																				
I	9	30	0	466	0	803	0	337	0	42	0	5 2	8 7	3 5	3 5	26				
			6	303	32 8	584	27 2	281	-16 6	48	+14	3 3	6 4	3 1	3 1					
			23½	253	45 7	478	40 5	225	-32 2	55	+32	2 8	5 3	2 5	2 5					

[illegible]

The hematocrit in the dogs of Group III showed a significant increase within four hours of the onset of distention. This increase averaged 42.5 per cent after 18 to 23 hours, while the undistended, obstructed dogs (Group II)

CHART 1
AVERAGE REDUCTION IN PLASMA VOLUME

- ① Reduction in PV of intact DOG after 24 hours under nembutal
- ② Reduction in PV of obstructed DOG after 24 hours under nembutal
- ③ Reduction in PV of obstructed and distended DOG after 24 hours under nembutal
- ④ Reduction in PV of obstructed and distended DOG after 4 hours under nembutal
- ⑤ Reduction in PV of obstructed and distended and strangulated DOG after 4 hours under nembutal

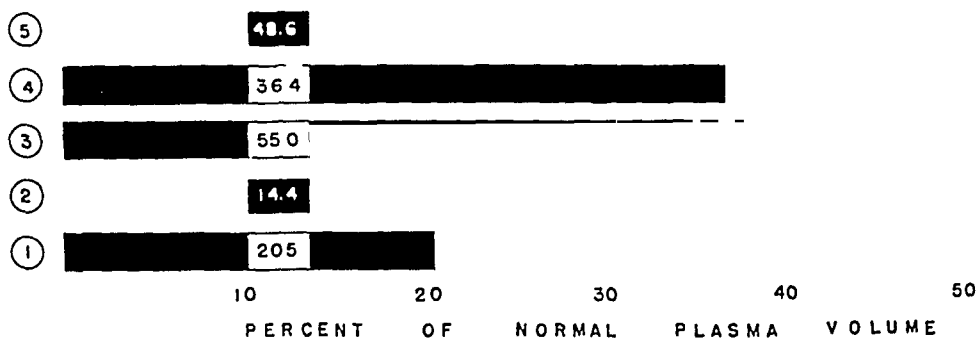
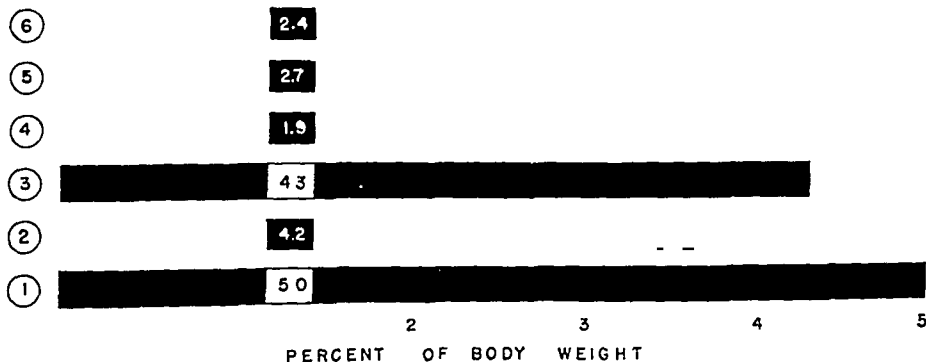


CHART 2
PLASMA VOLUME IN PER CENT OF BODY WEIGHT

- ① NORMAL
- ② PV of intact DOG after 24 hours under nembutal
- ③ PV of obstructed DOG after 24 hours under nembutal
- ④ PV of obstructed and distended DOG after 24 hours under nembutal
- ⑤ PV of obstructed and distended DOG after 4 hours under nembutal
- ⑥ PV of obstructed and distended and strangulated DOG after 4 hours under nembutal



showed a drop of 9 per cent and the intact, anesthetized dogs (Group I) an average rise of 8 per cent after the same interval. Table II shows the relatively small proportion of the average total blood volume loss that can be accounted for by the average loss in red cell volume when these losses are expressed in terms of percentage loss of body weight. For example, in

TABLE II
REDUCTION IN THE PLASMA, WHOLE BLOOD AND RED BLOOD CELL VOLUMES

	Average Loss of Plasma Volume		Average Loss of Total Blood Volume		Average Loss of Red Cell Volume		Average Change in Hematocrit		Average Survival								
	In Per Cent	In Per Cent of Body Weight	In Per Cent	In Per Cent of Body Weight	In Per Cent	In Per Cent of Body Weight	In Per Cent	In Per Cent	Period in Hours								
Intact, anesthetized dogs	With- out Fluid	With Fluid	With- out Fluid	With Fluid	With- out Fluid	With Fluid	With- out Fluid	With Fluid	With- out Fluid	With Fluid							
	24 hrs	22 4	18 6	0 9	0 8	6 6	18 0	0 5	1 6	+8 2	20	+0 4	0 8	+16	0	60	72
	48 hrs	27 5	1 2	0 9	13 1	28 0	1 1	2 4	0	37	0	1 5	+16	-12			
	72 hrs	19 0															
Obstruction, with- out distention	4 hrs	5 6	0 25	6 6	0 6	4 6	0 25	+1 0			32 5						
	23 hrs	14 4	0 68	12 8	1 1	10 9	0 90	-9 0									
	Obstruction, with distention	4-6 hrs	36 4	2 3	17 2	1 7	1 6	0 00	+37 8								
Obstruction, with distention and strangulation	13 hrs	43 6	2 4	26 0	2 5	16 4	0 20	+39 5									
	18-23 hrs	55 0	3 1	40 0	3 2	17 0	0 50	+42 5			20 8						
	4-4½ hrs	48 6	2 6	27 4	2 4	1 1	0 0	+39 0			13 5						

the obstructed and distended dogs, after 18 to 23 hours, the loss in whole blood volume is 32 per cent of the body weight. Of this amount only 0.5 per cent is due to loss of red cells.

Dehydration cannot be held responsible for the greater loss of plasma volume in the Group III dogs, since there was no noticeable loss of fluid into the intestinal lumen, bowel wall, or peritoneal cavity in any of the first three groups, while the dehydration due to lack of fluid intake, water of perspiration, and excretory an was presumably the same in all groups. Moreover, although Dogs 10 and 11 of Group III received 500 cc of 5 per cent glucose in physiologic saline during the course of their distention, their loss of plasma volume was as great after the same interval as in any of those in the same group which did not receive fluid.

It is consequently obvious that the plasma volume loss is due, at least in large part, to capillary leakage of plasma in a manner similar to that occurring in traumatic shock. *Therefore death from acute intestinal obstruction may be properly attributed to crucial changes in plasma volume due to the factor of distention alone.*

In the fourth group of three experiments in which spontaneous venous strangulation occurred after obstruction and distention, the average plasma loss after four and one-half hours was 48.6 per cent in comparison with an average loss, after the same interval, of 36.4 per cent in nine distended dogs of Group III without strangulation, and of 5.7 per cent in two obstructed dogs without strangulation or distention (Chart 1). Practically all of the loss of whole blood can, in these dogs, as in the Group III dogs, be accounted for by the loss of plasma. This suggests that the more rapid death of the strangulation obstruction dogs is due entirely to the more rapid loss of plasma. It is, therefore, probable that the clinical condition of strangulation obstruction (before the stage of peritonitis) constitutes a greater emergency than simple obstruction, not because of a fundamental difference in the pathologic physiology (e.g., "toxic proteoses"), but merely because of a quantitative difference in the rate of loss of plasma.

Discussion—The experimental contributions to the pathologic physiology of acute intestinal obstruction have been significant and useful, but it is all too clear in clinical practice that some vital factor still awaits clarification. Confirmation of the intoxication theory seems remote. The importance of noxious nervous stimulation cannot be ignored,^{11 12} but the available evidence regarding its rôle is conflicting.⁴ If the complicating features of strangulation and peritonitis are excluded from consideration, unrelieved obstruction remains a lethal disease in spite of the effective control of electrolytic imbalance and dehydration.

There is universal agreement that the central disturbing agent in simple acute intestinal obstruction is the increase in intra-intestinal pressure and that restoration of normal tension, whether by enterostomy, intubation and suction or inhalation of 100 per cent oxygen, will restore the patient to normal,

provided the clinical condition has not reached an irreversible stage, and the deficiency in water and electrolytes is corrected.

It is important to note that most of the experimental analyses of the effects of intra-intestinal tension are based on pressure levels which are far in excess of the values observed in clinical mechanical obstruction.⁷ Furthermore, it is somewhat surprising that these investigations have largely ignored the possible lethal effects of distention *per se* on the other organs of the peritoneal cavity, their lymphatics and blood supply, and on the dynamics of the general circulation.

It is a commonplace experience in the clinic and the experimental laboratory that uncomplicated intestinal obstruction (*i.e.*, without strangulation or peritonitis) is compatible with health so long as distention is prevented and the alimentary requirements are satisfied. A significant loss in plasma volume would not be expected and does in fact not occur in these circumstances. Two dogs with obstruction in the absence of distention showed, after 24 hours, an average plasma volume loss of 14.4 per cent, which is 0.7 per cent of the body weight. Two intact dogs, under light anesthesia, lost an average of 0.85 per cent of the body weight in plasma in the same interval.

But as soon as distention is produced, a rapid and extensive loss of plasma occurs. In four to six hours' time this averages 36.4 per cent of the normal plasma volume and in 18 to 23 hours 55 per cent, which is equivalent to 3.1 per cent of the body weight (Table II).

The marked difference induced by the distention factor alone is not due to a greater loss of water and electrolytes into the intestinal lumen, bowel wall, or peritoneal cavity, since the volume of fluid in these areas at autopsy was very small in all the dogs of this series except those with strangulation. Experiments now in progress to locate the site of the lost plasma and the mechanism by which distention causes the loss of plasma indicate that some of it, at least, may be incarcerated in the lower portion of the trunk and lower extremities as a result of mechanical obstruction to venous return, with resultant slow blood flow and capillary anoxemia, occasioned by the distended gut.

In two previous papers,^{2, 4} evidence was given that the survival time of cats exposed to varying degrees of intra-intestinal pressure was inversely proportional to the height of pressure. It is apparent from Table II that the survival time of the dogs in the four groups is inversely proportional to the extent of the loss of plasma. This suggests a probable correlation between the volume of plasma loss and the height of intra-intestinal pressure, although we did not observe such a correlation within the limited range of pressures used (15–30 cm).

And,¹³ by the vital red method of Brown and Rowntree,¹⁴ found a plasma loss of 31 and 50 per cent respectively in two of four dogs after several days of low small bowel obstruction. In the other two no significant change in plasma volume was noted. Those showing plasma loss had "gross dilatation and venous congestion" at autopsy, while the other two showed "moderate

dilatation" In the light of our experimental data, we would conclude from these statements that the degree of distention determined the extent of plasma loss. Auld's method of plasma volume determination is, however, open to the objection that the reliability of the method is questionable.

That the loss of plasma due solely to distention is of sufficient magnitude (2.34 per cent of the body weight[†] after 24 hours at a pressure of 15 to 20 cm of water) to cause death is clear from the work not only of Johnson and Blalock on dogs, but also of Elman and Cole,¹⁵ who found that cats die after a loss of plasma equivalent to 2.7 per cent of the body weight. Boyce, McFetridge, and Lampert¹⁶ found that death occurred in dogs after removal of an amount of whole blood equivalent to 4.56 per cent of body weight. Roome, Keith, and Phemister¹⁷ obtained nearly the same result, *i.e.*, 4.51 per cent. Harkins and Haimon¹⁸ and others have shown that much less loss of plasma than of whole blood can be tolerated by the experimental animal. A loss of red cells is better endured than an equivalent loss of plasma.

The marked loss of plasma in the distended animals is in conformity with the rise in hematocrit which, as early as four hours after the onset of distention, averages 37.8 per cent and, after 24 hours, averages 42.5 per cent. Since the loss of red cells is negligible (Table II), the hemoconcentration is due almost entirely to the loss of plasma. The implications of this observation in clinical therapy of obstruction is clearly that the use of whole blood for transfusion purposes is not only inferior to an equivalent volume of plasma, but has the disadvantage of adding red cells, which are not only not needed, but also increase the viscosity of the blood which is already too high. In determining whether the distended patient needs whole blood or merely plasma, the hematocrit should be the determining factor.

That the loss of plasma is an early and basic process in the syndrome of intestinal obstruction is evident from the extent of the plasma loss as early as the fourth hour after the onset of distention. *It is, consequently, proper to conclude that the replacement of plasma is as essential as any other therapeutic measure*, with the exception of the all important necessity of relieving the intra-intestinal pressure. If effective decompression cannot be achieved within a short time, the patient may die from lack of sufficient plasma volume.

The extent of the plasma loss after only four hours of distention in dogs provides a rough index of the amount of plasma which may be needed by a patient with obstruction who is on the verge of, or in the state of shock, *e.g.*, the average loss of plasma in dogs with obstruction and distention after four hours, while the animal is still in good condition, is 36.5 per cent. This percentage loss of plasma in an average individual weighing 70 Kg. is approximately 1,000 cc. If restored in the form of whole blood, 1,800 cc. would be required. The deficiency of current medical practice in this connection is therefore sufficiently obvious.

* This figure is derived by subtracting the average 24-hour plasma loss in Groups I and II from that of Group III.

Experiments are now in progress to determine the value of plasma transfusions in intestinal obstruction

Correcting dehydration, though useful and necessary, would seem to be a less vital matter at a critical stage in the process than the correction of the plasma deficiency

The least reliable guide to impending shock in animals with obstruction is the blood pressure curve which fails to show a shock level until just before death. Since a significant fall in plasma volume is demonstrable long before the blood pressure reaches shock level, reliance on the blood pressure is misleading

CONCLUSIONS

(1) Dogs with intestinal obstruction die more rapidly if distended than if not distended. If strangulation is superimposed on the distention, death occurs even more rapidly

(2) Distention of the obstructed intestine in dogs causes an early and progressive loss of blood plasma. The average loss of plasma volume reaches 36.4 per cent within four to six hours and 55 per cent within 24 hours. A 55 per cent loss of plasma is equivalent to 3.1 per cent of the body weight. Of this amount, 0.7 per cent can be attributed to dehydration, the remainder, or 2.38 per cent, is due solely to the deleterious influence of the distention on the general circulation. A loss of 2.38 per cent of the body weight in terms of plasma is sufficient to cause death

(3) Distention *per se* does not cause a loss of fluids into the intestinal lumen, bowel wall, or peritoneal cavity

(4) When strangulation is added to obstruction and distention, a 48 per cent loss of plasma occurs within four hours. It is suggested that strangulation obstruction in the absence of peritonitis causes death sooner than simple obstruction not because of a fundamental difference in the basic phenomena involved so much as because of a quantitative difference in the rate of loss of plasma

(5) The magnitude of the plasma loss due to distention alone is sufficient to indicate that the all important need for immediate decompression of the gut must be accompanied by a simultaneous administration of adequate quantities of plasma. The volume of plasma necessary to restore the normal plasma volume is far in excess of the amount commonly given to obstructed patients in clinical practice. The use of whole blood has disadvantages which make the use of plasma preferable

(6) The administration of plasma is necessary long before evidence of shock is indicated by the level of the blood pressure. The blood pressure curve is a misleading guide to the patient's condition

(7) The use of intravenous fluids and electrolytes is necessary but not so vital as that of plasma

(8) Distention is the central disturbing agent in uncomplicated obstruction. The mechanism by which it causes the loss of plasma is not clear. That

it is not because of a loss of fluids into the intestine and peritoneum (unless strangulation supervenes) is certain

(9) In evaluating the need for plasma or whole blood for the correction of the blood volume changes, the hematocrit should serve as a useful guide

REFERENCES

- ¹ Fine, J, and Levenson, W S The Effect of Foods on Postoperative Distention An Experimental Study *Am Jour Surg*, **21**, 184, 1933
- ² Rosenfeld, L, and Fine, J The Effect of Breathing 95 Per Cent Oxygen Upon the Intraluminal Pressure Occasioned by Gaseous Distention of the Obstructed Small Intestine *ANNALS OF SURGERY*, **108**, 1012, 1938
- ³ Fine, J, Banks, B M, Sears, J B, and Hermanson, L The Treatment of Gaseous Distention of the Intestine by the Inhalation of 95 Per Cent Oxygen *ANNALS OF SURGERY*, **103**, 375, 1936
- ⁴ Fine, J, Rosenfeld, L, and Gendel, S On the Role of the Nervous System in Acute Intestinal Obstruction *ANNALS OF SURGERY* (In Press)
- ⁵ Gibson, J G, and Evans, W A, Jr Clinical Studies of the Blood Volume I Clinical Application of a Method Employing the Azo Dye "Evans Blue" and the Spectrophotometer *Jour Clin Invest*, **14**, 301, 1937
- ⁶ Gibson, J G, and Evelyn, K A Clinical Studies of the Blood Volume IV Adaptation of the Method to the Photoelectric Microcolorimeter *Jour Clin Invest*, **17**, 153, 1938
- ⁷ Wangenstein, O H The Therapeutic Problem in Bowel Obstructions Chas C Thomas, Baltimore, 1937
- ⁸ Gibson, J G, Keeley, J L, and Pijoan, M Blood Volume of Normal Dogs *Am Jour Physiol*, **121**, 800, 1938
- ⁹ Gasser, H S, Erlanger, J, and Meek, W J Studies in Secondary Traumatic Shock IV The Blood Volume Changes and the Effect of Gum Acacia on Their Development *Am Jour Physiol*, **50**, 31, 1919
- ¹⁰ Johnson, G S, and Bialock, A Experimental Shock Study of the Effects of Loss of Whole Blood, of Blood Plasma, and of Red Blood Cells *Arch Surg*, **22**, 626, 1931
- ¹¹ Taylor, N B, Weld, C B, and Harrison, G K Experimental Intestinal Obstruction *Canad Med Assn Jour*, **29**, 227, 1933
- ¹² Herrin, R C, and Meek, W J Distention as a Factor in Intestinal Obstruction *Arch Int Med*, **51**, 152, 1933
- ¹³ Aird, I The Behavior of the Blood Volume in Intestinal Obstruction and Strangulation *Brit Jour Surg*, **26**, 418, 1938
- ¹⁴ Brown, G E, and Rowntree, L G The Volume of the Blood and Plasma W B Saunders Co, Philadelphia, 1929
- ¹⁵ Elman, R, and Cole, W H Loss of Blood as a Factor in Death from Acute Portal Obstruction *Proc Soc Exper Biol and Med*, **29**, 1122, 1932
- ¹⁶ Boyce, F F, Lampert, R, and McFetridge, E Occlusion of the Portal Vein An Experimental Study with Its Clinical Application *Jour Lab and Clin Med*, **20**, 935, 1935
- ¹⁷ Roome, N W, Keith, W S, and Phemister, D B Experimental Shock The Effect of Bleeding after Reduction of the Blood Pressure by Various Methods *Surg, Gynec, and Obstet*, **56**, 161, 1933
- ¹⁸ Harkins, H N, and Harmon, P H Plasma Exudation Loss of Plasma-Like Fluid in Various Conditions Resembling Shock An Experimental Study *ANNALS OF SURGERY*, **106**, 1070, 1937

A STUDY OF THE RESULTS OF MEDICAL TREATMENT OF DUODENAL ULCER

FORDYCE B ST JOHN, M D

AND

CHARLES A FLOOD, M D

NEW YORK, N Y

FROM THE DEPARTMENTS OF SURGERY AND MEDICINE OF THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA
UNIVERSITY, AND THE PRESBYTERIAN HOSPITAL IN NEW YORK

THE average patient with duodenal ulcer gives a history of intermittent symptoms with a tendency to recurrent attacks separated by intervals of time during which he is relatively free of gastro-intestinal symptoms. The study of a large series of patients with ulcer over a period of years reveals that the majority of cases under medical treatment are subject to recurrent symptoms of abdominal distress if the period of observation is continued over a long period of time. The difficulty of predicting the probability of recurrence in future years in a given individual with this disease constitutes a real problem for the clinician and often gives rise to uncertainty as to what type of treatment should be undertaken in a given case. The decision by the physician to subject his patient to surgery implies the assumption that under conservative treatment the patient has a poor prognosis and that following a given type of surgical treatment the prognosis would be better. Often surgery is undertaken because the patient and physician are both discouraged with the response to medical treatment but without the slightest degree of established probability that medical treatment would continue to be unsatisfactory in the future.

The present report is based upon a study of a series of conservatively treated patients with duodenal ulcer over a period of years. An attempt has been made to analyze certain factors which appear to determine prognosis in various types of cases, for the purpose of assisting in the solution of the question as to which patients with duodenal ulcer should be treated surgically and which patients have a satisfactory prognosis under medical therapy.

This study has been carried out by the members of the Combined Ulcer Clinic of the Presbyterian Hospital over a period of more than ten years. The patients under consideration have all, at one time or another, been admitted to the wards of the Presbyterian Hospital for symptoms attributable to duodenal ulcer and in this sense are a selected group. No private patients are included and only patients whose symptoms have been severe enough to warrant hospitalization during the period of observation in the Clinic are included.

The series consists of 225 patients. The diagnosis of duodenal ulcer was based upon the demonstration of a crater or a deformity in the first

portion of the duodenum on roentgenologic examination. It is realized that this criterion for diagnosis is not always accurate but it is the best available in the absence of an exploratory operation. The average follow-up period per patient has been approximately three years. The patients were seen in the Clinic usually at intervals of three months, oftener if they were having symptoms. Return visits to the Clinic were not contingent upon recurrence of symptoms. In fact, during the majority of revisits the patients had no significant gastro-intestinal complaints.

Ideally, the clinical course of a patient with duodenal ulcer should be recorded in terms of the amount of time in a given year in which he has had symptoms and the severity of the symptoms. This, however, is not practicable in an analysis of a large group of cases and in fact the statement of the patient is not sufficiently reliable to warrant such an attempt. We have expressed our results in terms of the presence or absence of symptoms in each year of observation in the Follow-Up Clinic. If the patient reported that he had had no ulcer symptoms over the period of an entire year this period was classified as satisfactory. If, however, the patient had any symptoms of ulcer, however mild, the entire year was classified as unsatisfactory (Chart 1). Symptoms such as belching or a mild sense of distention after meals were not interpreted as evidence of an active ulcer inasmuch as these complaints occur in so many normal individuals.

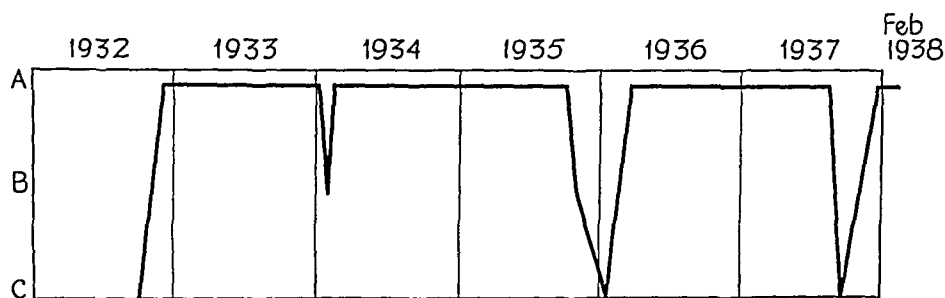


CHART 1—Illustrating the method of charting cases for group analysis (A) Freedom from ulcer symptoms (B) Moderate symptoms (C) Incapacitating symptoms

This patient was first hospitalized in October, 1932. He was symptom free in 1933, had moderate recurrences in 1934 and 1935 and severe recurrences in 1936 and 1937. Hence his record has included one satisfactory year, two years in which there were moderate recurrences and two years in which there were incapacitating recurrences.

The series includes 174 males and 51 females, a sex ratio of 3.5:1. Two hundred three of the patients were white, 19 were Negroes and three were Mongolians. The age distribution is shown in Table I.

TABLE I

AGE DISTRIBUTION

Second decade	4
Third decade	42
Fourth decade	79
Fifth decade	57
Sixth decade	26
Seventh decade	16
Eighth decade	1

The mean age of the patients when first seen in the Clinic was approximately 35. Inasmuch as all patients have been hospitalized in the wards of the Presbyterian Hospital, they represent the lower income group. Occupations of the patients are shown in Table II.

TABLE II
OCCUPATIONS

Laborers (skilled and unskilled)	78
Domestics (including housewives)	36
Office workers	26
Salesmen	23
Professional	18
Chauffeurs	14
Shopkeepers	9
Miscellaneous	21

There was of course wide variation in the duration of symptoms prior to observation. The duration of the disease preceding hospitalization varied from one to two days to more than 20 years according to the patients' histories. The number of patients whose symptoms were of recent onset was comparatively small. Thirty-one members of the group (14 per cent) gave a history of gastro-intestinal symptoms of less than two months' duration. The duration of illness exceeded one year in 172 cases (76 per cent).

Method of Treatment Employed—During hospitalization patients were kept in bed for approximately 18 days and placed upon a modified progressive Sippy regimen. In most instances alkalis were administered at two-hourly intervals. Mild sedatives, tincture of belladonna and nightly lavage were prescribed when indicated. Shortly before discharge from the hospital an ambulatory ulcer diet consisting of six feedings per day was begun. The patients were instructed to continue this diet after discharge and were also usually given alkaline powders to take if necessary for distress. An effort was made to secure the cooperation of each patient in continuing on an ambulatory ulcer regimen as long as possible, but inevitably there was wide variation in the length of time during which patients would continue to follow a restricted diet. Most individuals followed their diet for several months after discharge and the average patient continued to take interfeedings for from four to six months. A considerable proportion of patients remained on the diet for more than six months. Gradually, however, almost all patients began to omit the interfeedings and to eat a more liberal diet, although many continued to omit from their dietary regimen a selected number of foods such as pork, fried foods and spices.

Results for the Entire Group—Of the 225 patients included in this study, six have died as the result of ulcer, a mortality rate of 2.7 per cent. Three deaths were due to hemorrhage, one to rupture of the esophagus associated with vomiting, one to tetany and in one case the explanation for death was uncertain. Only seven members of the group have been subjected to surgery.

The total amount of time for which the entire group of patients has been followed is 842 years, giving an average of three and one-third years per patient. Individual follow-up periods have varied from a few months to 15 years.

During 503 follow-up years (or 60 per cent of the entire time) there has been complete freedom from symptoms of ulcer. In other words, our patients have remained symptom-free approximately one out of every two years. It should also be emphasized that most patients have been symptom-free during the major portion of those years in which recurrence took place. Furthermore, the majority of the recurrences have not been severe enough to interrupt normal activities and to incapacitate the individual. A more precise estimate of the severity of the symptoms is shown in Table III, in which the follow-up years are classified according to the severity of the symptoms.

TABLE III
ANALYSIS OF SEVERITY OF SYMPTOMS DURING FOLLOW-UP YEARS

Number of Cases	Years of Freedom from Ulcer Symptoms	Years in Which Moderate Recurrences Took Place	Years During Which Patient Had Incapacitating Recurrences	Total Follow-Up Years
225	503 (60%)	216	123 (15%)	842

It will be noted that the number of years in which patients were ill enough to be incapacitated was comparatively small, being only 15 per cent of the total (equivalent to one out of every seven years).

The foregoing figures, expressing results in terms of time, portray a fairly satisfactory follow-up for the group as a whole. However, they fail to show the tendency to recurrence in the large majority of cases. For this reason it is of interest to consider the proportion of cases who have remained

TABLE IV
ANALYSIS OF THE NUMBER AND PERCENTAGE OF PATIENTS IN THE GROUP REMAINING CONTINUOUSLY WELL OVER A PERIOD OF YEARS

Years of Follow-Up	2	3	4	5	6	7	8
Number of patients	140	90	79	59	43	33	25
Number of patients remaining free from recurrence	49	37	25	13	11	7	6
Percentage remaining free from recurrence	35%	40%	31%	22%	25%	21%	24%

* This is clearly shown when the results are analyzed by three-months periods instead of years. The results by three-months periods for the entire group are: Satisfactory periods—81 per cent, periods in which moderate recurrences took place—14 per cent, periods in which incapacitating symptoms occurred—5 per cent.

continuously symptom-free over a period of years. These results are shown in Table IV.

One hundred forty patients have been followed for more than two years. Sixty-five per cent of them had recurrences within the first two years of the follow-up period, leaving only 35 per cent who remained free from symptoms. The table shows the number of patients followed for more than two to more than eight years. Of the patients who were followed for more than five years, only 25 per cent of them have remained continuously free from symptoms. This tabulation illustrates the tendency for most of the patients to ultimately have a recurrence of the disease.

Patients with Persistent Pain under Hospital Management—The average follow-up expectancy in a group of patients who have received medical treatment for duodenal ulcer has comparatively little application to the individual case. The clinician is confronted with such individual problems as the patient with persistent pain in spite of hospital management, the patient who has had a gross hemorrhage without much pain, or the patient who has persistent pyloric obstruction not yielding to conservative therapy. Our entire group of patients has, therefore, been subdivided into smaller groups representing one or another of these clinical problems.

One of the commonest problems in the treatment of this disease is that presented by the patient who suffers from persistent abdominal pain in spite of ideal conservative treatment. We have found that our patients with

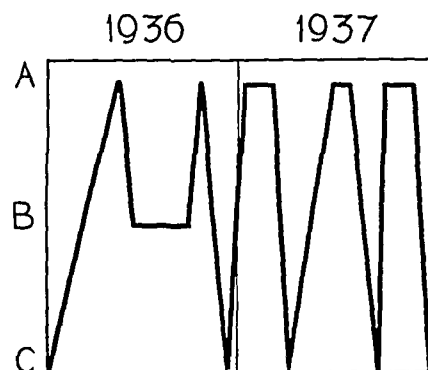


CHART 2—Persistent Pain During Hospitalization
O. D. (Unit No. 477771), was admitted in February, 1936, for pain due to duodenal ulcer. Pain persisted for 25 days in the hospital. The subsequent course has been very unsatisfactory and the patient has been hospitalized on four other occasions.

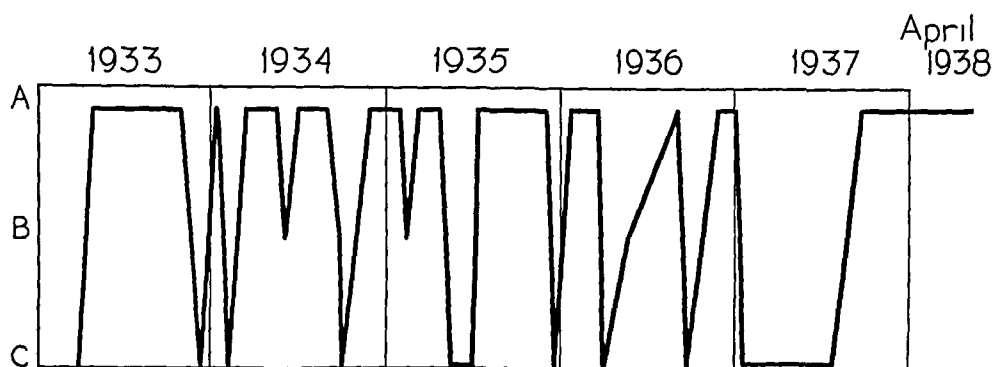


CHART 3—Persistent Pain During Hospital Treatment
E. L. (Unit No. 372307), was admitted in 1933 for duodenal ulcer of three and one-half years' duration. Pain persisted for three weeks while in the hospital. Subsequent course has been very unsatisfactory, there having been one or more incapacitating recurrences each year.

persistent pain under hospital treatment have a very unfavorable prognosis. Although not discharged from the hospital until their symptoms had completely subsided, those patients who had stubborn symptoms, yielding more slowly to treatment, suffered recurrences in succeeding years much more frequently than did the average patient (Charts 2 and 3). For purposes of

analysis, all patients who continued to have pain in the hospital on a modified Sippy regimen for more than two weeks and also any patient who suffered a recurrence of pain in the hospital after the first two weeks of treatment were classified in the persistent pain group. There were 57 such patients followed for an average period of three and one-half years. They remained free from symptoms of ulcer during only 30 per cent of the time (as compared with 60 per cent for the entire series). The details of analysis are shown in Table V.

TABLE V
RESULTS IN PERSISTENT PAIN GROUP

Satisfactory Years	Years in Which There Was Moderate Recurrence	Years in Which There Was Incapacitating Recurrence	Total
57 (30%)	87	49 (25%)	193 yrs

Not only was the frequency of recurrence much greater in this series of patients with persistent pain than in the average case, but the recurrences were more severe.

There are of course a number of patients in the persistent pain group whose individual results have been satisfactory, and the conclusion cannot be drawn that all patients with persistent or recurrent pain while under hospital treatment have a bad prognosis. In many of our cases, however, the results were so discouraging that surgical intervention should probably have been considered.

On further analysis, it was found that patients in this group with persistent pain who suffered a recurrence of symptoms during the first six months after discharge from the hospital had even more unsatisfactory results. In fact, the clinical course in such patients was so uneven and characterized by such frequent and severe recurrences that there remains no doubt that surgical treatment would have been preferable in most instances. There were 29 patients in the persistent pain group who had a recurrence within six months of discharge from the hospital. The follow-up results are shown in Table VI.

TABLE VI

Satisfactory Follow-Up Years	Years During Which Patients Had Moderate Recurrence	Years of Incapacitating Recurrence	Total Follow-Up Years
11 (14%)	44	23 (29%)	78

Careful analysis of the group with persistent pain revealed no other common characteristic which would have been suggestive of more serious disease. The average age was 42, not much older than the average in our

entire series of cases. The incidence of gross hemorrhage was not remarkable. Two-thirds (32) of the patients had never suffered from gross hemorrhage, nine had had a single gross hemorrhage and the remaining eight had had two or more hemorrhages. This incidence of hemorrhage is approximately of the same frequency as that of the entire series. Recognized psychiatric disease in this group was not particularly common. Four patients were diagnosed as having an anxiety neurosis and one patient had manic depressive insanity in a mild form. Only a few of our patients, however, have been studied by a psychiatrist.

The care with which dietary treatment was followed by this group of patients after discharge from the hospital varied, but in the majority of cases could be considered satisfactory, as only 13 of the 57 patients admitted having broken their diet during the first six months. Twenty-five patients reported careful adherence to the diet as prescribed, for at least six months after discharge, and in many instances the patients remained on this diet for more than a year. Ten patients followed the ambulatory ulcer diet for at least six months but omitted interfeedings at times. Information concerning

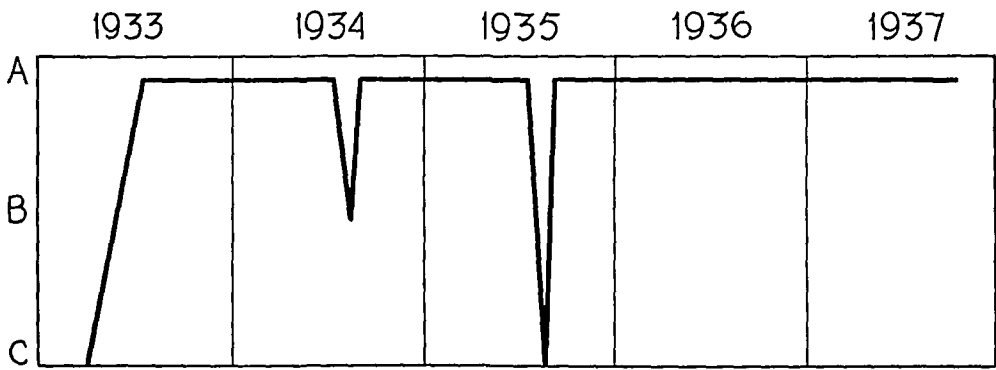


CHART 4—Immediate Response to Hospital Therapy
O. M. (Unit No. 372438), was admitted for a duodenal ulcer of 12 years' duration. No history of gross hemorrhage or obstruction. Subsequent course was fairly satisfactory. Patient has had one moderate and one severe recurrence in five years.

diet was incomplete on nine patients. In general it may be said that this group of patients were as conscientious about dietary treatment as can be expected. The results of treatment cannot be regarded as satisfactory.

Immediate Relief of Pain under Hospital Treatment—Inasmuch as there appeared to be a relationship between persistence of pain in patients with duodenal ulcer on hospital treatment and their prognosis, it was also of interest to analyze the results in those patients who had prompt relief of symptoms immediately after hospital admission. It was found that those patients who were admitted to the hospital because of abdominal pain and whose symptoms were relieved within 24 hours of admission appeared to have a very good prognosis (Charts 4 and 5). There were 36 cases falling within this group, namely, patients with relief of pain within 24 hours of admission and without any complication such as gross hemorrhage or pyloric obstruction. Some of the patients in this group had slight gastric

retention shown roentgenologically. The presence of a small barium residue on one examination, absent on the next examination, was not considered significant.

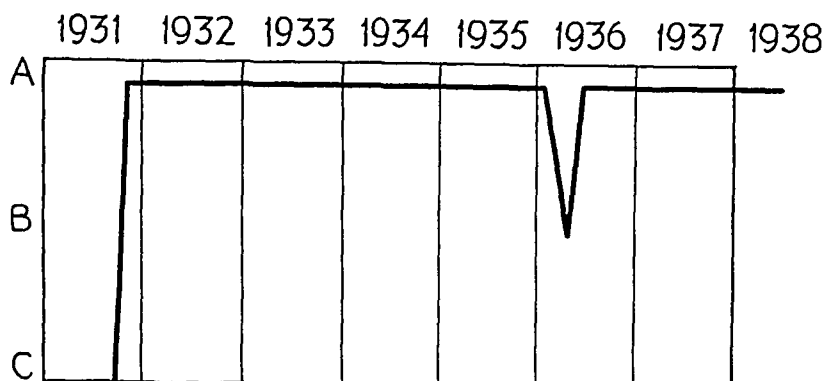


CHART 5—Immediate Relief of Symptoms After Hospitalization
C S (Unit No 318587), was admitted for symptoms of five years' duration. No history of gross hemorrhage or obstruction. Has been satisfactory for six out of seven follow up years.

This group of 36 cases has been followed for a total of 193 years, representing an average follow-up period of five and one-third years per patient. The results are shown in Table VII.

TABLE VII

Satisfactory Years	Years in Which There Were Moderate Recurrences	Years in Which There Were Incapacitating Recurrences	Total Years
148 (76%)	29	16 (8%)	193

Expressed otherwise, patients in this group suffered a recurrence of symptoms once in every four follow-up years. Incapacitating recurrences took place less than once in every ten years. It appears then that the patient who is admitted to the hospital for an uncomplicated duodenal ulcer and whose symptoms subside almost immediately after admission to the hospital has an excellent prognosis under medical treatment.

Gross Hemorrhage—Ninety-one patients in this series suffered from a gross hemorrhage at some time during their period of follow-up observation. Death resulted in three cases, a mortality rate of 3.3 per cent. There were five additional cases who gave a convincing history of hemorrhage but who have not bled since they have been under observation. In the majority of instances gross hemorrhage occurred only once. A small group, however, have suffered from repeated hemorrhages.

The patient who has had a series of gross hemorrhages from duodenal ulcer constitutes a serious therapeutic problem, involving the choice between surgical treatment and the continuation of medical therapy. There are only 18 patients in our series who were under observation after having had three

or more gross hemorrhages. This group is small because it has been the usual practice to treat such patients surgically and very few have been observed under continued medical treatment. The total follow-up period for this group of 18 patients has been 34 years, 60 per cent of which were satisfactory. Detailed results are shown in Table VIII.

TABLE VIII

Satisfactory Years	Years in Which Moderate Recurrence Took Place	Years in Which Severe or Incapacitating Recurrence Took Place	Total Follow-Up Years
20 (60%)	5	9 (26%)	34

The incidence of recurrence in our patients who have had multiple gross hemorrhages was no larger than the average for the entire series. At first hand, these results appear to be in conflict with the clinical impression generally held that patients with repeated hemorrhage due to duodenal ulcer have a poor prognosis. It should be noted, however, that the incidence of severe and incapacitating recurrence in these patients was large. In 26 per cent of the follow-up years the patients were incapacitated by recurrent symptoms of ulcer. It appears, therefore, that while the incidence of ulcer recurrence in patients with multiple hemorrhage is not greater than the average hospitalized case of duodenal ulcer, such patients are more apt to have very severe symptoms in subsequent attacks. In this sense, the outlook for the patient who has had multiple gross hemorrhages may be considerably worse than that of the individual who has an uncomplicated duodenal ulcer. This problem merits further study with a larger series of cases.

On the other side of the picture is the outlook for the patient who is suffering from an initial gross hemorrhage. His prognosis appears to be very satisfactory, particularly if the hemorrhage is not accompanied by pain or obstruction. There were 28 cases followed after admission to the hospital for an initial gross hemorrhage and who had no pain during hospitalization. This group includes both those patients who had never had any previous symptoms of duodenal ulcer and also those patients who had previously suffered from abdominal pain but who were not suffering from pain at the time of hospitalization. Results in these patients are among the best in our entire series (Table IX).

The question arises as to whether patients who have had a single gross hemorrhage are more apt to have recurrent bleeding in the future than are patients with duodenal ulcer who have never bled. Although our series of cases is too small to answer this problem positively it is of interest to note that of the 28 patients in this group admitted for an initial hemorrhage, seven (or 25 per cent) have suffered from subsequent hemorrhage during the

TABLE IX

Satisfactory Years	Years in Which There Were Moderate Recurrences of Symptoms	Years of Severe Recurrence
80 (76%)	15	11 (10%)

follow-up period In contrast, the incidence of hemorrhage during follow-up in patients who had not bled prior to hospital admission has been very low Of our group of 36 patients with uncomplicated duodenal ulcer who had immediate relief of pain on hospital admission, only one has had a subsequent gross hemorrhage

Another problem occasionally encountered in the hospital treatment of peptic ulcer is that of persistent bleeding Six patients in this series presented evidence of persistent bleeding during hospital treatment unassociated with persistent pain or obstruction The average patient admitted for gross hemorrhage from duodenal ulcer shows evidence of occult blood in the stool for five to seven days after admission For the purpose of the present analysis, patients who had a positive guaiac test in the stool after two weeks of hospitalization were classified as having persistent hemorrhage None of the six patients falling within this classification has had an unsatisfactory follow-up result after discharge from the hospital The number of patients, however, is too small to justify any conclusion concerning the prognostic significance of persistent hemorrhage in patients with duodenal ulcer

Persistent Pyloric Obstruction—There are very few patients in this series who had persistent obstruction during hospital treatment High grade pyloric obstruction in duodenal ulcer has long been an indication for surgical intervention A few patients, however, in this medically treated series had persistent obstruction throughout hospital treatment There were four patients who had at least a 50 per cent retention of the barium meal on roentgenologic examination at the end of six hours, persisting after at least two weeks of hospital treatment Hospital treatment consisted of rest, diet, belladonna and nightly gastric lavage The lavage was continued after the patients became ambulatory All four patients had very unsatisfactory follow-up results

Six other patients had an intermediate grade of pyloric obstruction as judged roentgenologically On entrance into the hospital, they were found to have a six-hour retention to 25 to 50 per cent of the barium meal This degree of obstruction persisted after hospital treatment The amount of obstruction in these cases was not as severe as in the first group Response to treatment was, however, not very satisfactory (Chart 6) Of the six patients, three had a satisfactory follow-up course and the other three continued to have symptoms of obstruction associated with pain

Discussion—The results of this survey indicate in a general way the prognosis for patients who are suffering from severe symptoms due to duodenal

ulcer The results do not apply to all patients with this disease, inasmuch as we have been dealing with a selected group We have purposely excluded from present consideration any patient under observation in the Clinic whose symptoms have never been severe enough to warrant hospitalization

Furthermore, our group does not include patients who have been under private care during the period of study Whether or not the prognosis in a group of individuals with duodenal ulcer whose economic status differs from that of persons eligible for clinic and ward care is a question that cannot be answered at the present time

The average period of follow-up per patient in our series is comparatively short, being only a little more than three years Our data, therefore, can only

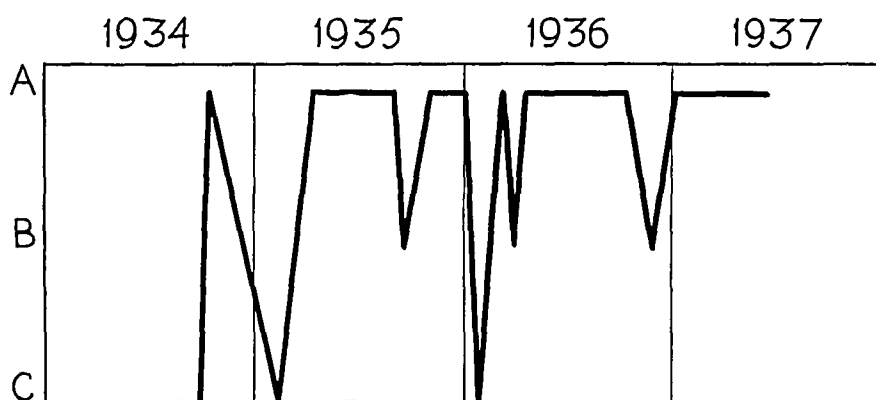


CHART 6—Persistent Obstruction

A. P. (Unit No. 419033), age 41, had initial symptoms 15 years ago. First admission, in October, 1934, was for moderate pyloric obstruction. On diet and lavage, the obstruction persisted (six hour barium residue of 25 per cent). Eventually, the patient became symptom free. His subsequent course has been one of frequent recurrences usually moderate in severity. At present, the patient still has slight obstruction demonstrable roentgenologically.

be applied with any degree of certainty in problems of immediate prognosis. Whether the expectancy of recurrence changes in a group of individuals under observation over a longer period of years will have to be determined by further study. There are indications, however, that in any large group of individuals with duodenal ulcer under conservative treatment, the number of recurrences remains approximately the same at any one time. Insofar as our follow-up studies have been carried, we have found that in any given six months' period, approximately 25 per cent of our patients suffer from symptoms attributable to ulcer, the remaining three-quarters of the group being symptom-free. This is true both of the first six months of follow-up after hospital treatment and of succeeding years.

Among the patients whom we have included in this study, the worst results were obtained in the group with persistent pain and the group with multiple hemorrhage. Results in our series of 57 patients with persistent pain during hospitalization have been so poor that in the future we feel that surgical therapy should be seriously considered for any patient who falls within this group. The combination of persistence of pain during hospital treatment and early recurrence after the patient becomes ambulatory has been followed by even worse results. In fact, our experience with almost every patient who

has fallen into this category has shown that it would have been wise to have subjected the patient to surgical intervention. Contraindications to surgery did not exist in the majority of patients in this group.

Our data concerning patients with multiple hemorrhage are rather surprising, in that they show no greater frequency of recurrence in this group than in the average case in the series. There is, however, no logical reason to assume that a patient who chances to bleed during a recurrence of ulcer on several occasions should be more prone to have frequent recurrences in the future. The important consideration is that when this type of patient does suffer a recurrence, the symptoms are more apt to be severe and the patient is again apt to have associated bleeding. It is this hazard that makes the patient with multiple hemorrhage a candidate for elective surgery.

Our number of patients with persistent pyloric obstruction associated with duodenal ulcer is too small to justify further comment. Persistent pyloric obstruction has long been one of the primary indications for surgical therapy in duodenal ulcer. Our very unsatisfactory experience with patients in this group under medical treatment is in accord with this general view. It should be pointed out, however, that marked pyloric obstruction frequently yields to treatment with bed rest and periodic gastric lavage. Patients of this type do not, of course, fall into the group with persistent obstruction. Operation for pyloric obstruction should usually be deferred until it has been demonstrated that such obstruction persists after adequate medical therapy.

It should again be emphasized that the majority of cases of duodenal ulcer, even in this selected series of patients with severe symptoms, respond very promptly to medical treatment in the hospital. It is the exceptional patient who continues to have pain or vomiting for two weeks or more after the institution of bed rest and frequent feedings. Certain it is that the disappearance of symptoms under treatment precedes by a considerable period of time the complete healing of the ulcer. The mechanism by which this relief of symptoms is effected is not entirely clear, but has been attributed in part to relief of pyloric spasm and neutralization of gastric acidity. The important rôle of mental relaxation which usually occurs following hospitalization should not be overlooked.

The correlation between the symptomatic picture and the pathologic lesion is also difficult in those patients with persistent pain followed by early recurrence. The question arises in these individuals as to whether there has been a persistence of the same ulcer or whether the original lesion has healed and a new ulcer has developed. Roentgenologic examination of the duodenum has not reached the degree of precision required to answer this problem. In view of the fact that many ulcers in the duodenum are not visualized roentgenologically (the examination often showing only a duodenal deformity), the radiologist is unable to determine whether patients in this group have a persistent or a recurrent ulceration. With future improvements in roentgenologic diagnosis or other methods of examination, it may become possible to segregate the group of patients with duodenal ulcer who have lesions which fail to heal.

on medical therapy. Such patients would be candidates for surgery. In all likelihood many of our patients with persistent pain under hospital treatment would fall within this group.

SUMMARY

(1) Follow-up results in the selected series of 225 patients with duodenal ulcer under medical treatment are reported.

(2) The majority of patients who were followed for more than two years developed recurrent symptoms. In most instances recurrences were mild and readily controlled by further medical therapy.

(3) Approximately 75 per cent of patients were symptom-free during each six months' period of follow-up observation.

(4) Detailed study revealed that certain selected groups of patients had an unsatisfactory prognosis in comparison with the other patients in the series.

(a) The majority of patients with persistent pain lasting for more than two weeks during hospital treatment had an unsatisfactory follow-up course. When patients of this type suffered an early recurrence of symptoms after discharge from the hospital, the results were even worse.

(b) Patients who had had three or more gross hemorrhages due to duodenal ulcer were not more prone to have recurrences than the average patient in the series. When recurrence took place, however, the symptoms were more apt to be severe.

(c) Prolonged medical treatment was undertaken in a few patients with persistent pyloric obstruction. The results were unsatisfactory.

(5) Certain groups of patients were found to have a prognosis which was better than average.

(a) Most patients with uncomplicated duodenal ulcer who had complete relief of pain within 24 hours of hospitalization had very satisfactory follow-up results.

(b) The majority of patients who were hospitalized for an initial gross hemorrhage without associated pain or obstruction had a very satisfactory follow-up course.

(6) Surgical therapy should be considered for patients falling into the categories enumerated under (4), namely, persistent pain, multiple hemorrhage and persistent pyloric obstruction.

INTERNAL BILIARY FISTULAE AND INTESTINAL OBSTRUCTIONS DUE TO GALLSTONES

ANDREW M. McQUEENEY, M.D.

BRIDGEPORT, CONN.

THE impaction of a gallstone as a cause of intestinal obstruction has long been recognized. An early, correct diagnosis has seldom been made. As a result, the patient is not sent to the hospital until in a dangerous condition. Wakeley and Willway⁷ state that "Most stones entering the intestinal tract are passed naturally, with no symptoms except the initial attack of biliary colic. Stones which are large enough to cause obstruction never pass the entire length of the common bile duct but ulcerate through from the gallbladder or a duct into the bowel."

There are two points which we wish to stress particularly relative to these cases. First, the intestinal obstruction, and second, the internal biliary fistula which is present. Not infrequently, a large stone has been found in the intestinal tract without having produced any untoward symptoms.

The records relative to the frequency of intestinal obstruction due to gallstones apparently vary rather widely. Osler¹⁸ reported 23 cases due to gallstones out of a total of 295, or 7.8 per cent. Vick,¹⁷ in a symposium on intestinal obstruction, in 1932, reported 47 out of 3,625 cases, or 1.3 per cent. Combining the statistics which we have gathered from various authors, it is found that out of a total of 7,232 cases of intestinal obstruction, 149 were due to gallstones, or 2 per cent of all obstructions. The mortality is in the neighborhood of 50 per cent and is largely the result of delay. The history is not typical of intestinal obstruction and the true diagnosis is difficult. We have records of 41 cases of complete or partial obstruction of the bowel during the past three years, two cases, or about 5 per cent, were due to gallstone impaction. The average age of all cases reviewed was 66 years, 80 per cent were females.

In practically every case in which the location of the obstruction was mentioned, it was within two feet of the ileocecal valve, most frequently about 12 inches from the cecum. In a large percentage of cases, the history of obstruction is intermittent. In most, there was an antecedent history suggesting gallstone colic, often several years previously, then recurrent attacks of so-called indigestion with distention, nausea and vomiting, with severe cramp-like pains which frequently ceased as suddenly as they had begun. The most common diagnosis was food poisoning. In many cases the history was vague, consisting of the occurrence of chills and fever, suggesting malaria or an infected gallbladder. After recovery from this, there followed recurrent headaches with vague abdominal pain, nausea and vomiting. These episodes were usually diagnosed as migraine. After a period of from three to 15 years

with symptoms suggestive of gallbladder disease, a complete obstruction of the bowel occurred. From the histories reviewed one would gather that the obstruction was incomplete at first. Relief is afforded by the stone moving back into a larger segment of the intestine by retroperistalsis. Finally, the stone is propelled into the narrow part of the ileum and becomes lodged. If recognized early, the operative removal of the stone is comparatively simple.

The stone finds entrance to the intestine by ulcerating through the gallbladder wall into some part of the intestinal tract, most frequently into the duodenum. Usually a short fistulous tract is found, sometimes there is a direct opening. The findings at autopsy, as reported by Courvoisier,²⁰ in 36 cases, are of interest in this connection. The fistula entered the duodenum in 25 instances, the ileum in one, into both the colon and duodenum in two, the colon in one, and no fistula was demonstrable in seven cases. In most instances, a dense mass of adhesions firmly bound the gallbladder and duodenum together, enclosing a cystoduodenal fistula. Of the 149 cases of internal biliary fistulae reported in the literature, the gallbladder was always involved. Therefore, while in theory a stone may ulcerate through the common duct into the intestine, not one case was found recorded. Every internal biliary fistula found was from the gallbladder to some part of the intestinal tract.

Bernhard² reported finding 109 internal biliary fistulae in 6,263 cases of surgical intervention upon the biliary passages, or 1.8 per cent. In most, there was an intermediate canal. The gallbladder opened into the duodenum in 56 instances, into the colon in 36, into the stomach in 12, and into several fistulous tracts in five. In addition to excision of the fistula, the principal bile tract was drained in 60 cases. The mortality was about 10 per cent.

There is a general impression that life expectancy is rather short after an internal biliary fistula has been established. This is largely due to the fact that in dogs an ascending infection through the bile passages occurs and death follows rather early. We may seriously question the truth of this observation as applied to man, if one reviews the statistics. We have had two cases in which an internal biliary fistula has existed, one for 19 years and the other for 15 years, without any evidence of alteration of normal health. In the presence of a fistula, the infection could directly enter the gallbladder. The duodenum, however, is relatively free of pathogenic bacteria.

Ehason and Johnson,¹ in a discussion of life expectancy subsequent to cholecystenterostomy, decided that cholecystogastrotomy or cholecystoduodenostomy has a definite place in the relief of common bile duct obstruction. Yet, they stress the point that the danger of ascending infection is so great as to preclude the adoption of the operation without careful deliberation. While the danger seems established in dogs, Robinson¹⁵ reports such anastomoses in both man and animals without resultant infection. It is known that man frequently survives for many years after such operations.

We wish to record two cases which have survived gallstone obstruction of the bowel, and lived with an internal biliary fistula, for 15 and 19 years, respectively, in normal health. In addition, there are two others with autopsy

findings, which occurred on the service of two confieres on the staff of St Vincent's Hospital. In all four of these cases the fistula was from the gallbladder to the duodenum. In each instance, the obstruction was within two feet of the ileocecal valve. The two fatal cases were admitted to the hospital six and seven days, respectively, after the onset of symptoms of obstruction. One reported having had stercoraceous vomiting four days before admission, she was considered too weak to warrant operation, notwithstanding which she survived for five days. The second was operated upon immediately after entering the hospital, she died in shock four hours after operation. There seems to be a similarity in the histories in nearly all cases studied. A detailed report of the symptoms in one case may assist in arriving at an earlier diagnosis.

Case Report—J. B., white, female, age 61, married, weight 170 lbs., was admitted to the hospital, May 11, 1918, with a history of complete obstruction of the bowel of 48



FIG 1—Photograph of the gallstone causing the intestinal obstruction.
FIG 2—Roentgenogram of the gastrointestinal tract showing diverticula at the site of attachment of the gallbladder to the duodenum.

hours' duration. Her previous history developed the fact that at the age of 16, she had had an attack of stomach trouble, evidenced by epigastric pain, nausea and vomiting, and had later become jaundiced. She had been constipated all her life, requiring laxatives, has three children, no genito-urinary diseases. For a period of years, she had been treated for episodes of "indigestion with severe headaches, nausea, vomiting and epigastric pain, lasting from one to three days", and always accompanied by abdominal distention and eructations. The last attack had occurred May 11, 1918, eight days before admission. The onset was not acute. There had been some distress in the epigastric region and she felt very feverish, was nauseated and had frequent vomiting spells. Headache was severe. Two days after the onset, pain in the upper abdomen to the left of the midline developed, and she had some fever and chilly sensations. The pain became intense on the third day, shooting from the epigastrium through to the back in the upper lumbar and interscapular regions. The abdomen had become distended and only small amounts of gas and feces could be passed. During the next few days nothing was passed per rectum, the pain

continued to be very severe and vomiting frequent. The patient became markedly distended and finally fecal vomiting ensued.

Physical Examination—On the eighth day after onset, the patient was in very poor condition and markedly dehydrated. Temperature 103° F, pulse rapid and weak. Face, chest and upper part of the abdomen of mottled purplish hue, while the lower extremities were cold and white. The abdomen was distended and the breathing was rapid but not labored. On palpation, a general soreness of the abdomen was elicited, with acute tenderness in the right lower quadrant. Otherwise, the physical examination was negative.

Laboratory Data—The urine showed a moderate amount of albumin and hyaline casts. The blood showed red blood cells, 3,600,000, hemoglobin, 70 per cent, white blood cells, 12,000, 90 per cent segmented forms, 8 per cent small lymphocytes, and 2 per cent large mononuclear. Wassermann test, negative. The blood picture was almost identical in all of the four cases reviewed here.

Operation—May 19, 1918. Under general anesthesia, the abdomen was opened through a six-inch paramedian muscle splitting incision.

Operative Pathology—The small intestines were greatly distended. The obstruction was found to be situated in the ileum, 12 inches from the ileocecal valve, and had resulted from the impaction of a large gallstone (Fig 1). The stone was removed and the intestine sutured. Further exploration showed a cobweb-like fibrosis or hepatitis of the right lobe of the liver, in the region of the gallbladder. The gallbladder was firmly attached, throughout its length, to the duodenum, and an opening between the gallbladder and the duodenum, about one and one-half inches in length, was identified. It felt much like the stoma produced by a gastro-enterostomy. A single cigarette drain was inserted. A blood transfusion of 500 cc was given and normal saline administered subcutaneously, repeatedly, to restore the chlorides. Convalescence was uneventful after the first 24 hours. The patient is still alive after 19 years and still has her biliary fistula, as was recently shown roentgenologically (Figs 2 and 3). She remains quite asymptomatic.



FIG 3—Roentgenogram after administration of dye in order to visualize the gallbladder. Seepage of the dye can be seen passing through the fistula into the duodenum.

CONCLUSIONS

All cases exhibiting severe abdominal pains, persistent vomiting and localized tenderness with moderate leukocytosis, will be in less danger from an exploratory celiotomy, despite negative roentgenologic findings, than by the expectant type of treatment. If a biliary fistula is found it need not cause too much concern.

REFERENCES

- ¹ Eliason, E. L., and Johnson, J. Surg., Gynec., and Obstet., 62, 50-56, January, 1936.
- ² Beinhard, R. Deutsch. Ztschr. f. Chir., 242, 493-506, 1934, 242, 736-756, 1934.
- ³ Beigerhoff. Roentgenpraxis, 7, 688-689, October, 1935.
- ⁴ McNamara, F. P., Faber, L. A., and Wesler, A. B. Jour. Iowa Med. Soc., 26, 45-47, January, 1936.

- ⁵ Wybert, A, and Gaire, E S Archives argent de enferm d ap digest de la nutricion, 11, 316-323, February and March, 1936
- ⁶ Skemp, A A, and Tiavnicck, F G Am Jour Surg, 32, 695-697, November and December, 1935
- ⁷ Wakeley, C P G, and Willway, F W Brit Jour Surg, 23, 377-394, October, 1935
- ⁸ Guttman, J H Am Jour Surg, 30, 548-550, December, 1935
- ⁹ Bloodgood, J ANNALS OF SURGERY, 49, 160, 1909
- ¹⁰ Turner, G Gray Post Graduate Med Jour, 2, 65-85, February, 1927 Idem Brit Med Jour, 20, 26, 1932
- ¹¹ Meyer and Spivack ANNALS OF SURGERY, 100, 148, 1934
- ¹² Souttar Brit Med Jour, 11, 1000, 1925
- ¹³ Fowweather and Collinson Brit Jour Surg, 14, 583, 1926-1927
- ¹⁴ Firor, W B, and Lewis, D Surgical and Roentgenological Department Johns Hopkins Hospital Report, January, 1933
- ¹⁵ Robinson Lancet, 218, 673, 1930
- ¹⁶ Leichtenstern Cited by Barnard in "Contributions to Abdominal Surgery"
- ¹⁷ Vick, R Brit Med Jour, 2, Part 2, 546, 1932
- ¹⁸ Osler System of Medicine, 1900
- ¹⁹ Barnaid, H L ANNALS OF SURGERY, 36, 161, 1902
- ²⁰ Courvoisier Path und Chm der Gallenwege, 1900

CHOLEDOCHUS CYST WITH A DOUBLE COMMON BILE DUCT¹

SEQUELAE AND COMPLICATIONS

S DANA WEEDER, M D

PHILADELPHIA, PA

CERTAIN prognostications as to future physiologic reactions were made in 1935, when Doctor Swaitley and I¹ reported a case of choledochus cyst with a double common bile duct. It is important to establish by direct evidence physiologic and surgical principles. In this way we are able to go forward with confidence in developing surgical procedures. The realization of these prognostications and certain interesting complications have prompted the present communication.

For those who may not be familiar with this interesting case, it might be well to review the important features, and again state our prognostications.

Résumé of Case Report¹—D M, male, age 4, was admitted to the Germantown Hospital in December, 1932. He was operated upon December 13, 1932, at which time a choledochus cyst was found and, after searching, what appeared to be a duct running from the porta hepatis to the duodenum. It was thought this duct was patulous, and would probably be adequate to carry sufficient bile to sustain life. Excision of the choledochus cyst was, therefore, performed. Because of the shocked condition of the patient, it was not possible to definitely establish the arrangement of the ducts. We felt rather certain, however, that they were arranged as shown in Figure 1 (B).

It seemed the right and left hepatic ducts were separate, and did not join, as is normal, but proceeded separately to the duodenum, and that the choledochus cyst and gallbladder were a part of the right hepatic duct, the distal end emptying into the duodenum which, I believe, was not patulous. This duct was ligated on both sides of the cyst.

We prognosticated then that (1) If the duct to the choledochus cyst was the right hepatic and it was ligated, atrophy of the right half of the liver must follow, bearing out the principle when the need for function ceases, function will cease and the part will undergo atrophy of disuse. (2) If atrophy of the right half of the liver occurs, then there should be a compensatory hypertrophy of the left half of the liver. (3) Compensatory hypertrophy of the left half of the liver will only occur if the left hepatic duct is sufficiently large to adequately take care of the increased secretion of bile. All of these conditions have come to pass. The patency and adequate size of the duct have been demonstrated, by the fact that, since a month after operation until the present time, there has never been any suggestion of jaundice. Atrophy of the right half of the liver and compensatory hyper-

¹ Presented before the Joint Meeting of the Philadelphia Academy of Surgery and the New York Surgical Society, at Philadelphia, Pa., February 9, 1938. Submitted for publication May 1, 1938.

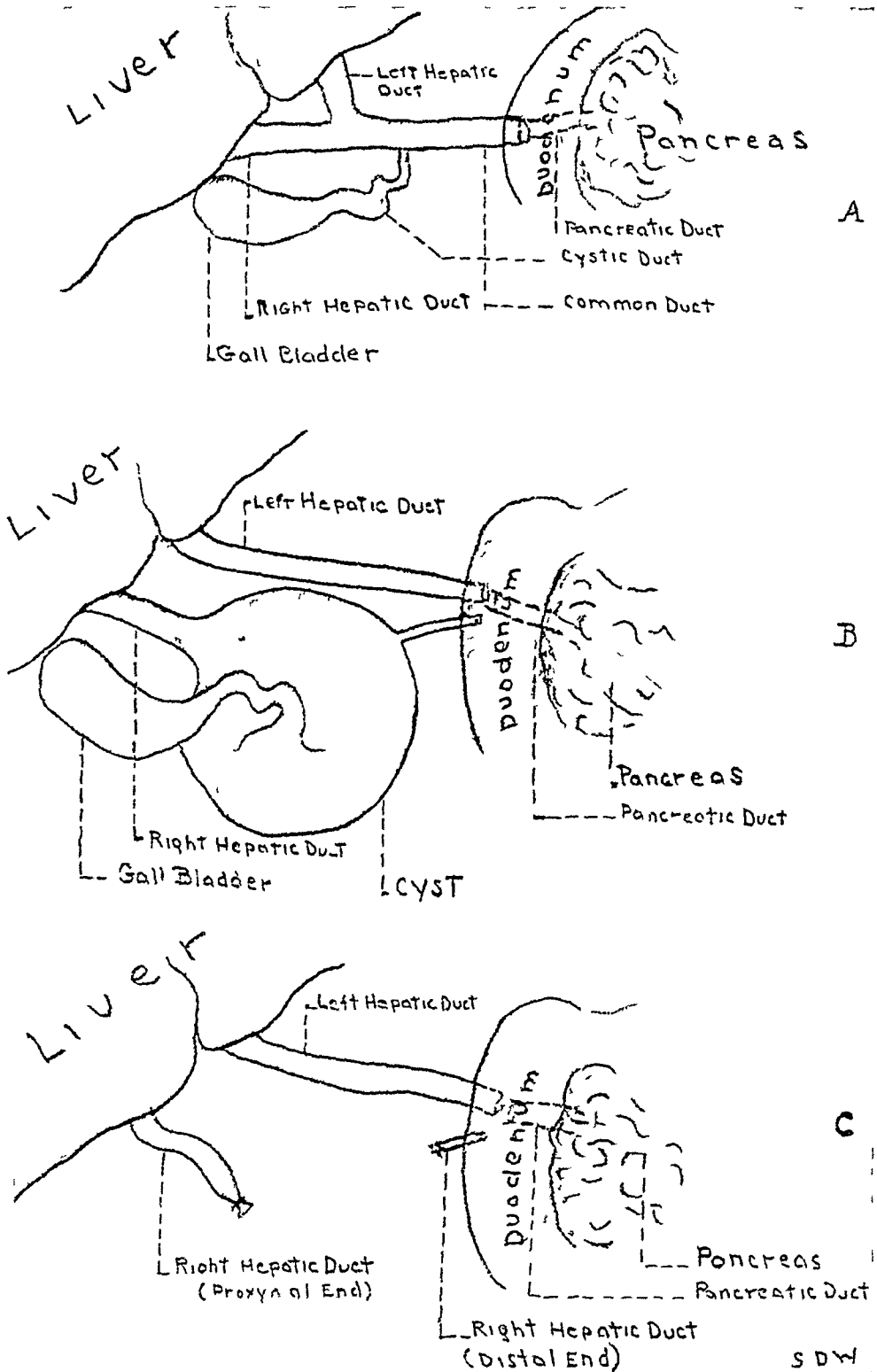


FIG 1—Diagrammatic sketches showing (A) Normal arrangement of bile passages (B) Present case of double common duct with choledochus cyst before operation (C) Resultant postoperative anatomy

trophy of the left half were demonstrated at the time of a subsequent operation, in 1936, when the abdomen was again opened

Subsequent Course—The patient remained entirely well until January 1, 1936, when he complained of malaise, some generalized pain and distention of the abdomen. The physical examination was negative except for pallor of the skin, a murmur at the apex of the heart, pulse 128, considerable enlargement of the veins of the abdomen and some ascites. Two masses were palpable, one, extending three fingers' breadth below the ensiform, the other, about two and one-half fingers' breadth below the left costal margin. One was thought to be the liver, the other the spleen.

Laboratory Data—Red blood cells, 1,400,000, Hb, 15 per cent, white blood cells, 4,000, thrombocytes, 74,000. All the white blood cells were normal in size, shape and staining. The red blood cells showed polychromasia, there were occasional nucleated cells but the majority were pessary cells, some microcytes and poikilocytosis. There was no stippling.

The coagulation time was five minutes, bleeding time, four minutes, fragility began at 0.3 per cent, not complete in 0.5 per cent. Van den Bergh test. Delayed positive direct reaction, indirect 1.8 units, strength of bilirubin, 9.8 mg per liter. Sedimentation rate, 38 Mm in 60 minutes. The stool was weakly positive for blood.

Treatment—Ten transfusions by the direct method were given between January 3, 1936, and February 3, 1936, with very slight improvement in any of the blood elements. On the latter date, there were red blood cells 2,300,000, Hb 26 per cent, white blood cells 3,900, thrombocytes 82,000. A diagnosis of splenic anemia was made and a splenectomy was performed, February 5, 1936.

The opportunity was offered at this time to verify our previous prognostications. The right lobe of the liver was atrophied, the left lobe greatly hypertrophied. There was a moderate amount of cirrhosis of the liver. The bile duct was visualized in the gastrohepatic omentum passing from the porta hepatis to the duodenum. There was some increase of peritoneal fluid. The veins of the peritoneum and the omentum were greatly enlarged. The spleen filled the left half of the abdomen. It was removed without difficulty, and a blood transfusion of 150 cc given.

Pathologic Examination—The spleen showed "advanced chronic splenitis with endarteritis and almost complete obliteration of arterioles. Moderate obliterating thrombophlebitis. Almost complete obliteration of splenic architecture. It measures 145x110x56 Mm. The capsule is smooth, the notch prominent. It is a mottled brownish-red, there are areas of dusky purple. The pulp is firm and the splenic follicles are prominent, here and there are small pin point hemorrhages."

Subsequent Course—The patient's convalescence was uneventful excepting that, by April 10, 1936, we were suspicious that he might be developing leukemia, because of a lymphadenopathy and a white cell count that reached 31,000. However, with the aid of two more transfusions and some hypodermic injections of liver, he was discharged with a rather fair blood count—red blood cells 3,800,000, white blood cells 14,900, Hb 69 per cent, thrombocytes 700,000 (May 3, 1936).

Many blood counts were made during the following year, which showed variations occurring mostly in the white cells. The white blood cell counts were always above 14,000 and on two occasions reached 26,000, with a drop in the neutrophils to 25 per cent, an increase in the lymphocytes to 66 per cent and an increase of eosinophils to 5 per cent. The thrombocyte counts were very high, ranging from 500,000 to 800,000.

The child was otherwise well, attended school regularly and played as other children until September 23, 1937, when he complained of great fatigue and nausea, and vomited a large amount of bright red blood. He vomited blood again, September 25, 1937, and was readmitted to the hospital. Examination showed the skin pale, there was restlessness, and he was apparently very sick. There was abdominal distention and tenderness in the upper abdomen. Blood count: red blood cells 750,000, Hb 22 per cent, white blood cells 27,500, neutrophils 77 per cent, lymphocytes 17 per cent, mononuclears 6 per cent, marked anisocytosis, many macrocytes and microcytes, some nucleated red blood cells and polychromasia. Five transfusions, by the direct method, were given.

After the bleeding had been stopped for some time, a gastro-intestinal series "showed a large stomach with no filling defect, duodenal cap does not fill out well on the serial films. Considerable amount of barium in the small bowel at the one-hour examination, and a normal duodenal cap. Small six-hour retention with normal duodenal cap." Twenty-four-hour examination showed the barium in the cecum, transverse colon and sigmoid, which appeared stringy.

The greatest amount of free hydrochloric acid (5) was found in the second specimen. The highest total acidity (26) was found in the fifth specimen. Occult blood was weakly positive, negative for bile and starch. The stool was strongly positive for blood. Coagulation time was four minutes, bleeding time five minutes and venous clotting time six minutes.

His convalescence was fairly smooth, and he was discharged November 11, 1937. Blood count: red blood cells 3,005,000, Hb 42 per cent, white blood cells 16,700, thrombocytes 198,000, reticulocyte count of less than 1 per cent.

Since his discharge he has steadily improved. There has been no evidence of gastro-intestinal or other bleeding, and his blood count December 3, 1937, was: red blood cells 4,350,000, Hb 59 per cent, white blood cells 17,900, neutrophils 64 per cent, lymphocytes 30 per cent, mononuclears 6 per cent, thrombocytes 920,000. On February 7, 1938, it showed: red blood cells 3,950,000, Hb 63 per cent, white blood cells 10,100, polymorphonuclears 48, lymphocytes 37, mononuclears 12, eosinophils 2, basophils 1 per cent.

In conclusion, certain questions are raised for which we have not the answers. It is interesting, however, to speculate on them. Are these complications—the blood dyscrasia and the gastro-intestinal hemorrhage—both the result of back pressure on the portal system, resulting from the atrophy of the right half of the liver and the fibrosis in the remaining part? Has the back pressure produced changes in the normal physiology of the spleen, resulting in alterations in function of the reticulo-endothelial system? If this be so, does Banti's disease originate in the liver, and is it the result of changes in that organ produced by toxins, either infectious, metabolic or disturbed endocrine secretions?

We have been inclined to believe the hemorrhage originated in either varicose veins of the stomach or esophagus.

REFERENCE

- ¹ Swartley, W. B., and Weeder, S. D. Choledochus Cyst with a Double Common Bile Duct. *ANNALS OF SURGERY*, 101, 912-920, March, 1935.

DISCUSSION —DR ALLEN O. WHIPPLE (New York) Doctor Weeder has presented a most unusual and interesting patient. First, the anomaly described is unique. In Kehr's¹ Textbook on Biliary Surgery and Schachner's² article describing the collected anomalies of the gallbladder and ducts,

in which he summarizes Kehr's studies, there is no mention of a double common bile duct

Schachner collected 76 anomalies of the biliary tract, of which 14, or 18 per cent, were multiple. Of these 76 cases, eight showed anomalies of the bile passages. There were two cases of double cystic duct, five with anomalous arrangement of the hepatic duct, and one case of absence of the common duct in an infant.

There is no doubt that far more of these anomalies are seen than those reported in the literature. Every surgeon of experience in biliary tract surgery has seen them. It is important to emphasize the point of adequate exposure for visualization of the gallbladder and gastrohepatic omentum. If an anomaly of the blood supply to the gallbladder is found, an anomaly in the duct arrangement should be looked for and vice versa.

The second point, and to the speaker even more interesting, is the subsequent history of this case, with the development of a splenomegaly in the presence of a cirrhosis with portal bed obstruction. We have been greatly interested in our Combined Spleen Clinic, at the Presbyterian Hospital, in the pathogenesis of splenomegaly. In some patients, undoubtedly intrahepatic portal obstruction results in a splenomegaly. In other cases, with thrombophlebitis of the splenic or portal vein proximal to the liver, splenomegaly develops without liver changes. In still others, portal bed irritation, as seen in schistosomiasis and in dogs following silica powder injections of a portal radical, splenomegaly is associated with cirrhosis. In all of these several pathogeneses, the clinical picture is Banti's syndrome, *i e*, an anemia, a leukopenia, a low platelet count and an enlarged spleen.

REFERENCES

- ¹ Kehr, Hans. *Die Praxis der Gallenwege Chirurgie*, Bd I and II
- ² Schachner, A. *ANNALS OF SURGERY*, 64, 419, 1916

DR S. DANA WEEDE (closing). We drew the conclusions in the first paper on this subject that probably there were more cases of double ducts in association with choledochus cyst, that a search should be made for a duct running through the gastrohepatic omentum, and if it be found and thought to be patulous, then removal of the choledochus cyst should be undertaken. This would result in a lowering of the present mortality of 28 per cent resulting from choledochocystoduodenostomy.

The child was otherwise well, attended school regularly and played as other children until September 23, 1937, when he complained of great fatigue and nausea, and vomited a large amount of bright red blood. He vomited blood again, September 25, 1937, and was readmitted to the hospital. Examination showed the skin pale, there was restlessness, and he was apparently very sick. There was abdominal distention and tenderness in the upper abdomen. Blood count: red blood cells 750,000, Hb 22 per cent, white blood cells 27,500, neutrophils 77 per cent, lymphocytes 17 per cent, mononuclears 6 per cent, marked anisocytosis, many macrocytes and microcytes, some nucleated red blood cells and polychromasia. Five transfusions, by the direct method, were given.

After the bleeding had been stopped for some time, a gastro-intestinal series "showed a large stomach with no filling defect, duodenal cap does not fill out well on the serial films. Considerable amount of barium in the small bowel at the one-hour examination, and a normal duodenal cap. Small six-hour retention with normal duodenal cap." Twenty-four-hour examination showed the barium in the cecum, transverse colon and sigmoid, which appeared stringy.

The greatest amount of free hydrochloric acid (5) was found in the second specimen. The highest total acidity (26) was found in the fifth specimen. Occult blood was weakly positive, negative for bile and starch. The stool was strongly positive for blood. Coagulation time was four minutes, bleeding time five minutes and venous clotting time six minutes.

His convalescence was fairly smooth, and he was discharged November 11, 1937. Blood count: red blood cells 3,005,000, Hb 42 per cent, white blood cells 16,700, thrombocytes 198,000, reticulocyte count of less than 1 per cent.

Since his discharge he has steadily improved. There has been no evidence of gastro-intestinal or other bleeding, and his blood count December 3, 1937, was: red blood cells 4,350,000, Hb 59 per cent, white blood cells 17,900, neutrophils 64 per cent, lymphocytes 30 per cent, mononuclears 6 per cent, thrombocytes 920,000. On February 7, 1938, it showed: red blood cells 3,950,000, Hb 63 per cent, white blood cells 10,100, polymorphonuclears 48, lymphocytes 37, mononuclears 12, eosinophils 2, basophils 1 per cent.

In conclusion, certain questions are raised for which we have not the answers. It is interesting, however, to speculate on them. Are these complications—the blood dyscrasia and the gastro-intestinal hemorrhage—both the result of back pressure on the portal system, resulting from the atrophy of the right half of the liver and the fibrosis in the remaining part? Has the back pressure produced changes in the normal physiology of the spleen, resulting in alterations in function of the reticulo-endothelial system? If this be so, does Banti's disease originate in the liver, and is it the result of changes in that organ produced by toxins, either infectious, metabolic or disturbed endocrine secretions?

We have been inclined to believe the hemorrhage originated in either varicose veins of the stomach or esophagus.

REFERENCE

- ¹ Swartley, W. B., and Weeder, S. D. Choledochus Cyst with a Double Common Bile Duct. *ANNALS OF SURGERY*, 101, 912-920, March, 1935.

DISCUSSION—DR ALLEN O. WHIPPLE (New York) Doctor Weeder has presented a most unusual and interesting patient. First, the anomaly described is unique. In Kehr's¹ Textbook on Biliary Surgery and Schachner's² article describing the collected anomalies of the gallbladder and ducts,

in which he summarizes Kehr's studies, there is no mention of a double common bile duct

Schachner collected 76 anomalies of the biliary tract, of which 14 or 18 per cent, were multiple. Of these 76 cases, eight showed anomalies of the bile passages. There were two cases of double cystic duct, five with anomalous arrangement of the hepatic duct, and one case of absence of the common duct in an infant.

There is no doubt that far more of these anomalies are seen than those reported in the literature. Every surgeon of experience in biliary tract surgery has seen them. It is important to emphasize the point of adequate exposure for visualization of the gallbladder and gastrohepatic omentum. If an anomaly of the blood supply to the gallbladder is found, an anomaly in the duct arrangement should be looked for and vice versa.

The second point, and to the speaker even more interesting, is the subsequent history of this case, with the development of a splenomegaly in the presence of a cirrhosis with portal bed obstruction. We have been greatly interested in our Combined Spleen Clinic, at the Presbyterian Hospital, in the pathogenesis of splenomegaly. In some patients, undoubtedly intrahepatic portal obstruction results in a splenomegaly. In other cases, with thrombophlebitis of the splenic or portal vein proximal to the liver, splenomegaly develops without liver changes. In still others, portal bed irritation, as seen in schistosomiasis and in dogs following silica powder injections of a portal radical, splenomegaly is associated with cirrhosis. In all of these several pathogeneses, the clinical picture is Banti's syndrome, *i e*, an anemia, a leukopenia, a low platelet count and an enlarged spleen.

REFERENCES

- ¹ Kehr, Hans. *Die Praxis der Gallenwege Chirurgie*, Bd I and II
² Schachner, A. *ANNALS OF SURGERY*, 64, 419, 1916

DR S DANA WEEDE (closing) We drew the conclusions in the first paper on this subject that probably there were more cases of double ducts in association with choledochus cyst, that a search should be made for a duct running through the gastrohepatic omentum, and if it be found and thought to be patulous, then removal of the choledochus cyst should be undertaken. This would result in a lowering of the present mortality of 28 per cent resulting from choledochocystoduodenostomy.

DOUBLE GALLBLADDER WITH TWO CYSTIC DUCTS AND TWO CYSTIC ARTERIES

CLYDE L WILSON, M D

JAMESTOWN, N Y

WHILE variation from the usual distribution of the biliary ducts is common, duplication of the gallbladder is relatively rare, occurring about once in every 3,000 to 4,000 human beings. A satisfactory embryologic explanation of these anomalies in man is difficult or impossible.

Boyden,¹ in 1926, undertook an investigation in order to ascertain the comparative and embryologic background for the comparison of human anomalies of the biliary system. In his study of comparative anatomy, 10,000 autopsies were performed upon domestic animals (Table I).

TABLE I
STUDY OF COMPARATIVE ANATOMY OF 10,000 AUTOPSIES PERFORMED UPON DOMESTIC ANIMALS SHOWING ANOMALIES OF THE GALLBLADDER

Animals	Number	Anomalies	Per Cent
Cats	2,568	315	12.0
Calves	2,555	95	3.5
Sheep	2,560	30	1.17
Pigs	2,572	13	5

In man, however, Boyden found that data regarding gallbladder anomalies revealed a startling infrequency. Inquiries sent to 11 of the largest hospitals showed but one anomaly among 9,221 autopsies. A request for case reports from roentgenologists revealed only three anomalies. Thus, 19,191 examinations showed only four anomalies. Searching the literature, he found 15 case reports of accessory gallbladders, to which he added five other instances which had not been reported, making a total, up to 1926, of 20 cases of double gallbladder with two cystic ducts. Of these cases, four had separate ducts, which later united into a common canal before entering the common duct and nine cases could not be classified regarding the arrangement of the ducts. The remaining three case reports were of the bilobed gallbladder variety and were (1) A drawing in Cruveilhier's *Anatomy*, 1864, showing an anomaly but not accompanied by any history, (2) a case reported by Deaver and Ashhurst, 1914, stating that the specimen was "bilobed" one large lobe discolored and gangrenous and containing one calculus, the other lobe normal, and (3) a case reported by Ullman, which had been diagnosed by cholecystography, but which on exploratory operation failed to reveal more than one cystic duct. Therefore, from 1674 to 1926 reports of only 20 cases of double gallbladder are to be found in the literature.

Slaughter and Trout,⁵ in 1933, reviewed the literature in an abbreviated manner, including Boyden's article, and found 11 other case reports of double gallbladder and added a case of their own. This was of a female, age 32, who, at operation, was found to have the cystic duct adherent to the duodenum. The gallbladder contained no calculi. After removal of the gallbladder, a second gallbladder, 5x1 cm in diameter, was found in the liver substance with a separate duct leading from it. This second gallbladder appeared atrophic but was otherwise normal, it was, therefore, not removed. Later the patient was given dye but the remaining gallbladder could not be visualized.

This list of 12 cases, in addition to the 20 cases reported by Boyden, made 32 cases of anomalies of the gallbladder reported up to March, 1933. The entire series of cases reported by Slaughter and Trout was composed of double gallbladders.

Weiss,⁶ in 1935, reported three cases of double gallbladder diagnosed by cholecystography, two with calculi. He pointed out that in order to be included under the classification of double gallbladder, each gallbladder should have its own cystic duct, thus differentiating it from the bifid gallbladder, in which the cavities are distinctly separate but communicate with the common duct through a single cystic duct. He modified Boyden's classification of the aberrant hepatic vesicles, and placed them into the following four groups:

(1) *Ductular* —Derived from supernumerary vesicles from either the hepatic, cystic, or common bile ducts. Two cavities are present, each having its own cystic duct. This type is found chiefly in man but is present also in cats.

(2) *Bilobed* —Formed by initial subdivision of the primitive gallbladder bud. Two cavities communicate with the common bile duct through a single cystic duct. This type is found chiefly in cats but is also found in man.

(3) *Diverticular* —Resulting from persistence of cavities and septa in the gallbladder bud. One large cavity, communicating with one or more smaller cavities, found chiefly in ungulates.

(4) *Trabecular* —A vesicular outgrowth of liver trabeculae, common in cattle and sheep, but of doubtful occurrence in humans.

Gross,³ in 1936, reviewed the literature and found 147 cases of congenital anomalies of the gallbladder and reported a case of double gallbladder found at the autopsy of a child, age three years and three months. At no time during the patient's life had there been symptoms of disease of the biliary tract. One of the accessory gallbladders was found in the substance of the liver and its duct communicated with the midportion of the main hepatic duct. The other, or primary gallbladder, was on the undersurface of the liver and its duct entered the common duct at the junction of the hepatic and common ducts. Both cystic ducts were present.

Therefore, with the 20 cases of double gallbladder reported by Boyden, the 12 reported by Slaughter and Trout, the three reported by Weiss, and one by Gross, there had been 36 cases reported up to January, 1936.

A case of double gallbladder with two cystic ducts, found at operation,

is herewith presented It is interesting not only because of the anomaly, but because of the several types of gallbladder disease present in the specimen removed

Case Report—Hosp No 17525 B W, white, female, married, age 55, was admitted to the Jamestown General Hospital, December 14, 1936, complaining of severe epigastric pain associated with nausea and vomiting She stated that about 2 A M she was awakened by severe epigastric cramp-like pain radiating to between the scapulae and associated with nausea and vomiting Since its onset, the pain had gotten steadily worse and was not relieved by a hypodermic of morphine She had had repeated attacks of similar pain, although not so severe, during the past 20 years During the past year,

FIG 1

FIG 2

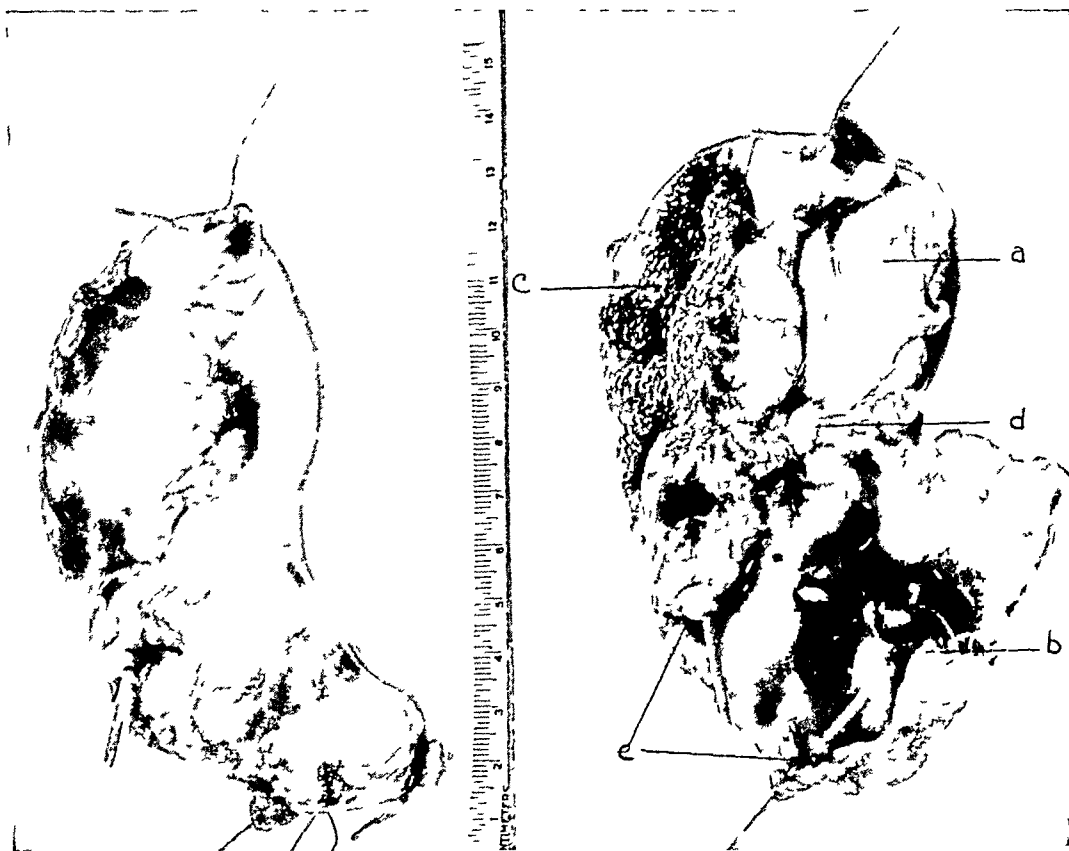


FIG 1—Photograph of the unopened specimen. Wooden probes in cystic ducts

FIG 2—Photograph of the open specimen, with lettering corresponding to Figure 3 (a) Empyema cavity, (b) cavity containing five gallstones, (c) "strawberry" gallbladder, (d) thick septum of fibrous tissue separating empyema cavity (a) from cavity containing gallstones (b), (e) cystic ducts. The pale, smooth lining of cavities (a) and (b) shows the effect of the chronic inflammation, and their thick, edematous walls is evidence of the acute inflammation

these attacks had become more frequent and more severe The last one, two months previous to admission, lasted four days, during which she was treated with morphine She had never been jaundiced She had noticed that fatty or greasy foods caused her indigestion

Except for repeated attacks of epigastric pain her past history was irrelevant She had had six pregnancies, none of which was associated with pain similar to that of her present illness She had gained 25 pounds in weight during the past year and had noticed some shortness of breath on exertion and swelling of the ankles

Physical Examination revealed an acutely ill, very cooperative, short, obese, white female, five feet, four inches tall, weighing 214 pounds Temperature 98.2° F, pulse 82,

DOUBLE GALLBLADDER

blood pressure 150/82 There was no jaundice The abdomen was thick-walled and pendulous There was muscle spasm and acute tenderness to pressure just to the right of the midepigastrium No masses were palpated

Laboratory Data—Urine clear, straw colored, sp gr 1.020, very faint trace of albumin, sugar negative, microscopic examination showed few pus cells WBC, 16,400, polymorphonuclears, 85 per cent, lymphocytes, 10 per cent, large mononuclears, 5 per cent *Clinical Diagnosis*—Acute cholecystitis and obesity

The patient was given 1,000 cc of 5 per cent glucose by hypodermoclysis and morphine to control the pain The following day, 36 hours after the onset of the attack of pain, she was operated upon

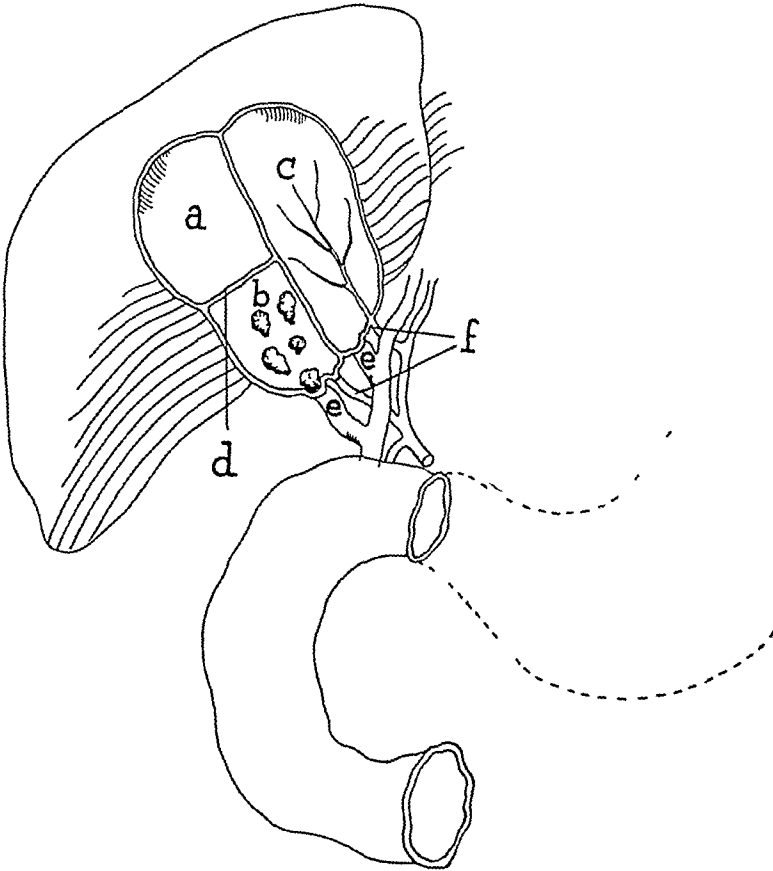


FIG 3—Diagrammatic drawing of specimen removed (a) Empyema cavity, (b) acutely inflamed cavity containing gallstones, corresponding to the pouch of Hartmann, (c) second gallbladder, separated from the first by a common wall, seat of cholesterosis, (d) septum of chronic inflammatory tissue separating empyema cavity (a) from acutely inflamed cavity containing stones (b), (e) cystic ducts, (f) cystic arteries

Operation and Operative Pathology—Doctor Wilson Under nitrous oxide-ether anesthesia the abdomen was opened through a right transverse subcostal incision On opening the peritoneal cavity a large gallbladder presented itself, resembling a markedly dilated and thickened small intestine in color and appearance The omentum was adherent to the anterior surface The portion nearest the duodenum was acutely inflamed and the entire gallbladder was thickened The pouch of Hartmann resembled, and was about the size of the average gallbladder

Dissection was started from above downward, stripping the gall bladder from the liver bed, leaving enough peritoneum to cover the raw surface Leading into the gallbladder below the pouch of Hartmann was a cystic duct, accompanied by a cystic artery A stone was impacted in this cystic duct, this was milked into the gallbladder and the duct and artery were clamped, divided, and ligated separately On dissecting back along

FIG 4

FIG 5

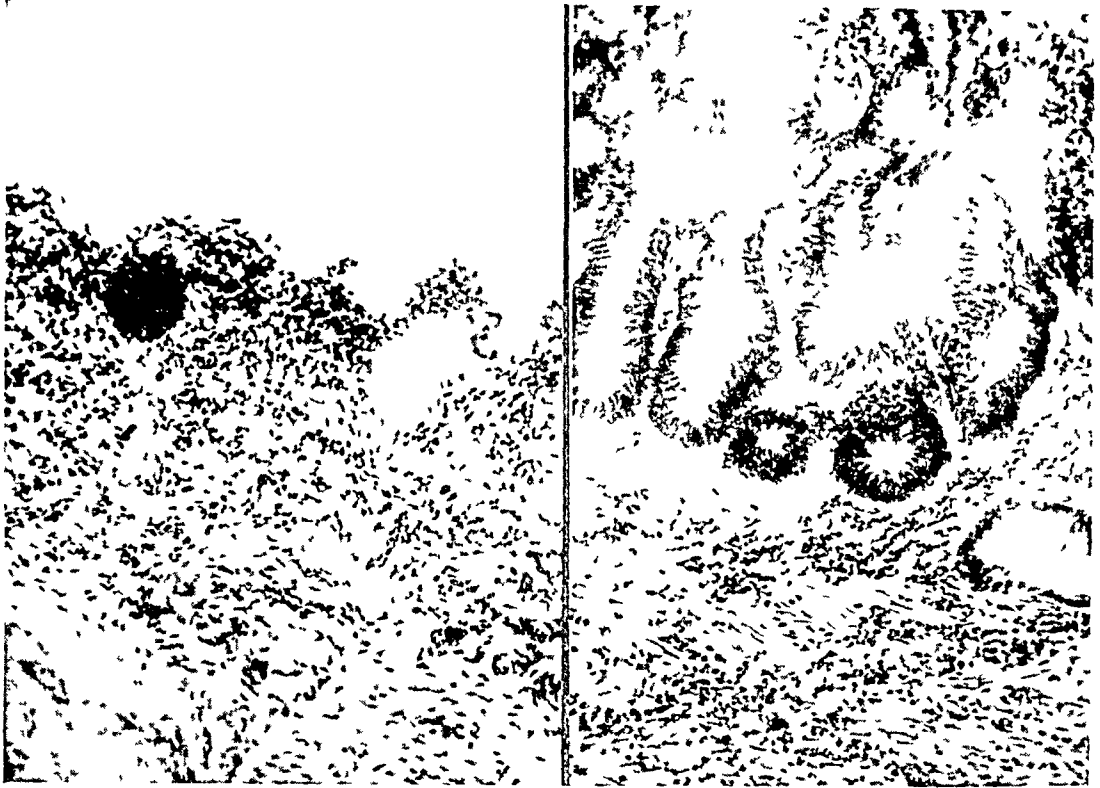


FIG 4—Photomicrograph of section taken from empyema cavity (Figs 2a and 3a) showing obliteration of glandular mucosa together with a marked inflammatory reaction in subcutaneous area

FIG 5—Photomicrograph of section taken from the acutely inflamed cavity (Figs 2b and 3b) showing acute inflammation in the submucous area extending down into the muscle

FIG 6

FIG 7

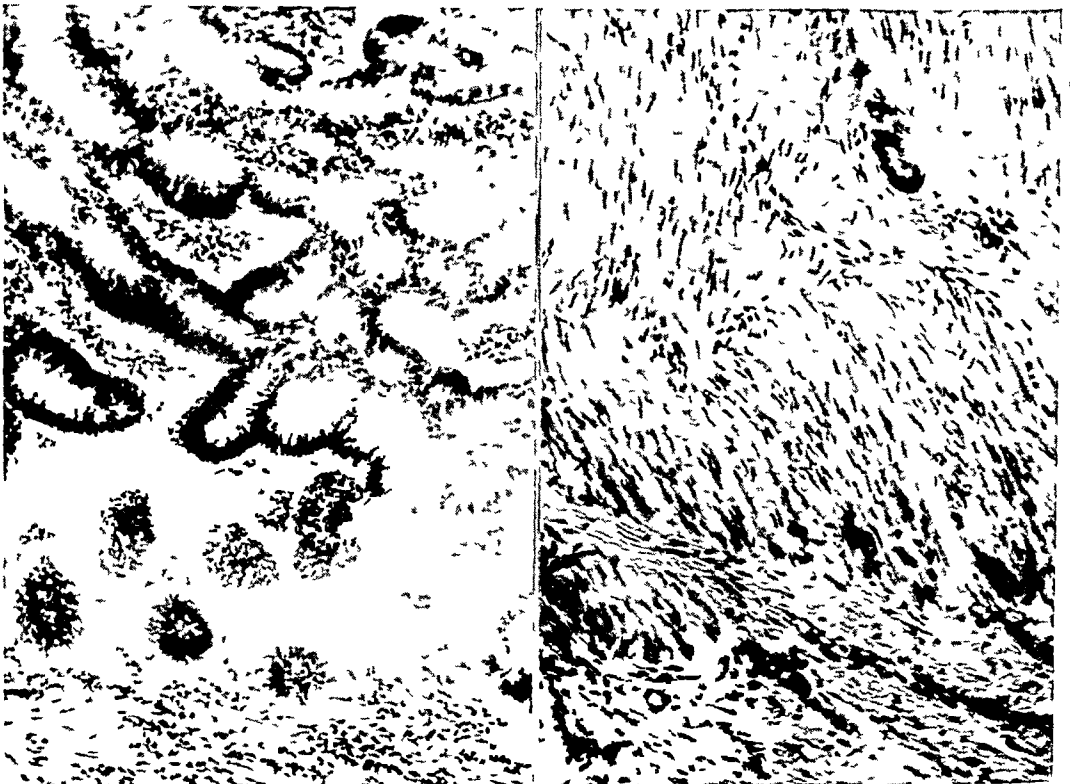


FIG 6—Photomicrograph of section taken from cavity (Figs 2c and 3c) showing proliferation of glands showing papillomatous growth. Grossly the mucosa was covered by deposits of cholesterol giving it the appearance of a typical 'strawberry' gallbladder

FIG 7—Photomicrograph showing leukocytic infiltration of the muscular coat

the common duct toward the liver, a second cystic duct and artery were discovered, about 25 cm from the first one. This duct was normal in appearance and size. It, and the accompanying artery, were separately clamped, divided, and ligated, after which the gallbladder was removed. There was a large acutely inflamed lymph node at the junction of the second cystic duct with the common duct. Peritoneum was sutured over the raw liver bed, a cigarette drain was placed to the foramen of Winslow, and the incision was closed in layers about it, and a small rubber tissue drain introduced into the median angle of the incision.

Pathologic Examination—Gross. On opening the gallbladder it was found to be divided by a longitudinal septum into two distinct cavities, with the septum as a common wall for each organ, each cavity having a separate duct and artery supply.

The part of the gallbladder corresponding to the pouch of Hartmann (Figs 2b and 3b) contained five faceted calcium-bilirubin calculi varying in size from 0.7 to 1 cm in diameter. This cavity contained about 30 cc of black bile, in which were flecks of pus, it was supplied by a cystic duct and accompanying artery. Separating this cavity from a similar one (Figs 2a and 3a) was a septum of tough fibrous tissue (Figs 2d and 3d). This second cavity contained about 30 cc of thick, gray pus and its walls were thickened and inflamed. The cystic duct nearest to the liver led into a third cavity (Figs 2c and 3c) separated from the distal side by a common wall. Its walls were moderately thickened, though not nearly as much as those of the other two cavities. It had a bluish-gray appearance from the outside. About 40 cc of thick, black bile was removed. On the soft mucosal surface there were areas of cholesterol deposits which gave this part of the gallbladder a typical "strawberry" appearance. The specimen measured 11.7 by 4.8 cm in diameter. The entire gross specimen was sent to the State Institute for the Study of Malignant Disease, Buffalo, N. Y., for microscopic examination.

Microscopic Examination—Dr A. A. Thibideau. "Sections of the gallbladder wall taken at various areas show an acute inflammatory reaction extending throughout the wall. In some areas there is a marked papillary proliferation of the glandular epithelium lining the gallbladder. There is some question as to the presence of malignant changes in these areas as the proliferation extends into the lumen of the gallbladder and apparently does not invade the gallbladder wall proper. *Pathologic Diagnosis*—Acute cholecystitis and papilloma of the gallbladder."

Postoperative Course—The patient made an uneventful recovery from the operation. At no time was her temperature above 100° F. She was discharged on the fifteenth day postoperative.

COMMENT—It is to be regretted that no roentgenologic examination of this double gallbladder was made. The patient had not been seen by the author before the last attack of pain for which she sought relief, and no roentgenograms had been taken prior to that attack. It is the author's practice to treat acute cholecystitis by early operation, believing that such a procedure avoids much suffering, prevents liver damage, and is less dangerous. Certainly, the patient is better off following an operation which is preceded by only a short period of illness, of a few hours' duration, than she would be if forced through a period of fever, pain, nausea, vomiting, with restricted food intake and the other discomforts of "the cooling off" process.

SUMMARY

(1) A brief review of the literature on double gallbladder is presented there having been 36 cases reported up to the present time, indicating the rarity of this anomaly in man.

(2) A case of double gallbladder with two cystic ducts and two cystic arteries is presented. The gross pathologic examination shows the five stages of gallbladder disease: (1) Acute cholecystitis, (2) chronic cholecystitis, (3) cholelithiasis, (4) cholesterosis, and (5) empyema. The microscopic examination showed, in addition, a papilloma of the gallbladder.

BIBLIOGRAPHY

- ¹ Boyden, E. A. The Accessory Gall Bladder, an Embryological and Comparative Study of Aberrant Biliary Vesicles Occurring in Man and the Domestic Mammals. *Am Jour Anat*, **38**, 177-231, November 15, 1936.
- ² Beaver, M. G. Variations in the Extrahepatic Biliary Tract. *Arch Surg*, **19**, 321-326, August, 1939.
- ³ Gross, R. D. Congenital Anomalies of the Gall Bladder. Review of 148 Cases, with Report of a Double Gall Bladder. *Arch Surg*, **32**, 131-162, January, 1936.
- ⁴ Schackner, A. Anomalies of the Gall Bladder and Bile Passages with Report of a Double Gall Bladder and a Floating Gall Bladder. *ANNALS OF SURGERY*, **37**, 419-433, 1916.
- ⁵ Slaughter, F. G., and Trout, H. H. Duplication of the Gall Bladder. *Am Jour Surg*, **19**, 124-125, January, 1933.
- ⁶ Weiss, S. Diseases of the Liver, Gall Bladder, Ducts, and Pancreas. Their Diagnosis and Treatment, pp 102-112, Paul B. Hoeber, Inc., 1935.

•

THE EFFECT OF DEHYDROCHOLIC ACID UPON BILIARY PRESSURE AND ITS CLINICAL APPLICATION

R. RUSSELL BEST, M.D., N. FREDERICK HICKEN, M.D., AND
ALISTER I. FINLAYSON, M.D.

OMAHA, NEB.

DEPARTMENT OF SURGERY, UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE, OMAHA, NEBRASKA

FOLLOWING cholecystectomy in some instances, symptoms develop which are referable to partial obstruction of the common duct, either by a calculus overlooked at the time of operation or by a mucous plug, blood clot or inspissated bile. In the past it has been necessary on many occasions to re-operate upon the patient to relieve such an obstruction, but during the last 18 months, we have been carrying out studies on the cholangiographic demonstration of such obstructing agents and a nonoperative method of removing them.

Fundamentally, the method we have used consists in increasing the pressure behind the foreign body and relaxing the sphincter area in front of it, thereby permitting the object to pass out of the duct and into the duodenum, unless it is a stone of too large a caliber. There are two methods of increasing the pressure behind the obstructing agent. One, depends upon the presence of a T-tube or catheter in the common duct and consists in irrigating the duct with sterile normal saline or other solutions, using a syringe to increase the pressure. The other method depends upon an increased flow of bile at an increased pressure in response to a choleretic drug such as dehydrocholic acid.

The latter method has the distinct advantage that a fistula or drainage tube is not necessary, and it may, therefore, not only be applied as a therapeutic measure in all cases postoperatively, but may be used as an added step in the routine nonoperative management of gallbladder disease. By employing dehydrocholic acid, the pressure may be exerted more or less continuously over a given period and at any momentary relaxation of the sphincter, automatically or through the use of drugs, the foreign body may escape from the duct.

Oddi,¹⁷ in 1894, attempted to discover what pressure the sphincter might withstand without relaxing or "breaking" open. He found this to be 675 Mm of water. Heidenham and Friedlander disputed his finding and describe a pressure of 200 Mm. In 1926, Potter and Mann¹⁸ summarized the observations of many workers on the pressure withstood by the sphincter of Oddi in various animals (Table I). The average pressure found by these workers seems to rest between 100 and 150 Mm of water. It is difficult to correlate Oddi's finding with those of the other authors.

Koster and Shapiro,¹¹ in 1936, devised a manometer to determine the pressure withstood by the sphincter of Oddi, which they found to be 230 Mm of

water. The base line was determined by actually measuring the depth of the common duct below the skin surface.

TABLE I
SUMMARY OF OBSERVATIONS ON BILIARY PRESSURE
(Potter and Mann¹⁸)

Observer	Animal	Pressure in Millimeters
Oddi	Dog	675
Archibald	Dog	180-330
Judd and Mann	Dog	100-150
Mann	Cat, dog, goat, rabbit, guinea-pig	75-100
	Gopher rat	30
Jacobson and Gydesen	Dog	150
McWhorter	Dog	100-200
Cole	Dog	150
Winkelstein and Aschner	Dog	60-65

Mann¹³ was curious as to what relationship might exist between the presence or absence of a gallbladder and the sphincter tone. He, therefore, made a series of pressure studies in animals normally having a gallbladder and another series in animals normally lacking this organ. In the former group, fell the dog, cat, goat, rabbit, striped gopher and guinea-pig. The sphincter resistance in these animals was found to average 100 Mm. of water. In the second series only one animal was used, the gopher rat. Its resistance was found to be 30 Mm. at the maximum.

Following these studies on the normal pressure required to overcome the tone of the sphincter of Oddi, it developed, naturally, that studies concerning the effect of drugs, foods, and other agents upon the sphincter would be undertaken.

Lueth,¹² in 1931, studied the effect of duodenal peristalsis upon the sphincter "break" pressure. He found that pilocarpine, which caused hypertonus in the duodenum, interfered with relaxation of the sphincter and brought about an increase in the "break" pressure from 20 to 60 Mm. of water. He also noted an influx of bile into the duodenum during its relaxation which ceased with active peristalsis.

Potter and Mann,¹⁸ in 1926, found the average duct pressure in the dog to be 120 Mm. of water. They noted that fasting brought about a reduction in this pressure and that milk caused a marked rise. They also commented on the fact that cholecystectomy produced an increase in the common duct pressure to 235 Mm., whereas, Judd and Mann⁹ had previously stated, in 1917, that after cholecystectomy the sphincter of Oddi did not have a pressure resistance as high as that previous to operation.

Elman and McMaster,⁶ in 1926, claimed to have demonstrated that fasting caused greater resistance to the flow of bile into the intestine, while feeding resulted in lowered resistance to this flow. They determined biliary pres-

suies four to six hours after feedings and determined 100 to 120 Mm of water to be the normal range, while after fasting, the pressure would range between 150 and 250 Mm. After a meal, pressure often reached as low as 50 Mm. They noted that even the smell of food lowered the resistance to biliary flow. Twenty to 25 minutes after a meal, they observed a "secondary increase" in resistance to bile flow.

McGowan, Butsch and Walters,¹⁴ in 1936, studied the effect of different drugs upon the sphincter of Oddi and the resultant changes in biliary pressure, noting the onset of pain on one occasion with a water column 160 Mm above the skin surface. They found that after administering morphine the pressure rose from 200 to 350 Mm of water and that amyl nitrite caused complete disappearance of the pressure and relief from pain.

Best and Hicken,² in 1935, although not measuring the pressure within the common duct during their cholangiographic studies on spasm of the sphincter, assumed and stated that the pain was due to the increased ductal pressure occasioned by the spastic occlusion of the lower end of the common duct. They presented cholangiograms showing relaxation of the spastic sphincter following administration of 1/100 G1 of nitroglycerin beneath the tongue.

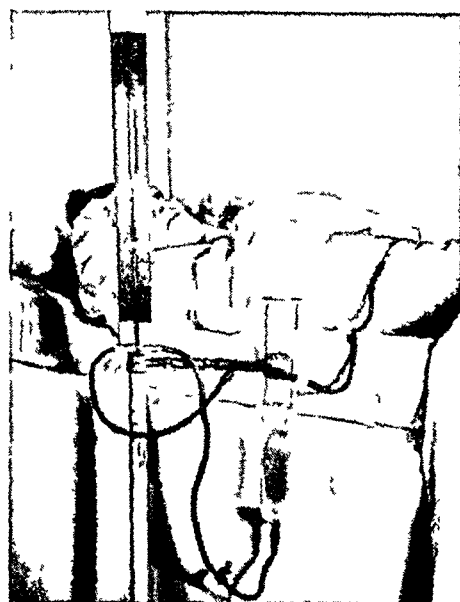


FIG. 1.—The manometric equipment used in determining the pressure within the common duct.

Koster and Shapiro¹⁰ criticized the readings of McGowan, because the base line used was the skin surface, but so long as the same base line was used each time, the relative change in pressure would be significant.

Doubilet and Colp,⁵ in 1937, stated that, in the absence of the gallbladder, meals have no effect upon sphincter tone. They found, however, that duodenal lavage, using a solution of magnesium sulfate, produced a relaxation of the sphincter. Hydrochloric acid placed in the duodenum caused a spasm of the sphincter which could be relieved with atropine. Morphine, however, produced a spasm of the sphincter which persisted over three hours and was not relieved by atropine. This appears logical when one considers the pharmacologic action of atropine, which causes paralysis of the parasympathetic nerve endings, and that morphine directly stimulates the smooth muscle.

Elman and McMaster⁷ found that the secretory pressure of the liver is a rather definite entity, above which biliary secretion stops. Herring and Simpson,⁸ in 1907, noted the average maximum bile pressure in the dog, cat and monkey as 300 Mm. The highest they recorded was 373 Mm in a cat. Similarly, McMaster, Brown and Rous,¹⁵ in 1923, stated that bile ceased to be secreted when the duct pressure reached 350 Mm of bile.

It might be well at this time to clarify the terms "secretory pressure of the

liver," the so-called "normal common duct pressure" and the "break pressure" of the sphincter area. We feel, after reviewing the observations of others, that the secretory pressure varies between 200 and 300 Mm of water. The pressure within the common duct must necessarily vary with and be dependent upon the amount of bile secreted into the duct with a given liver secretory pressure. This, in turn, must be dependent upon the resistance en-

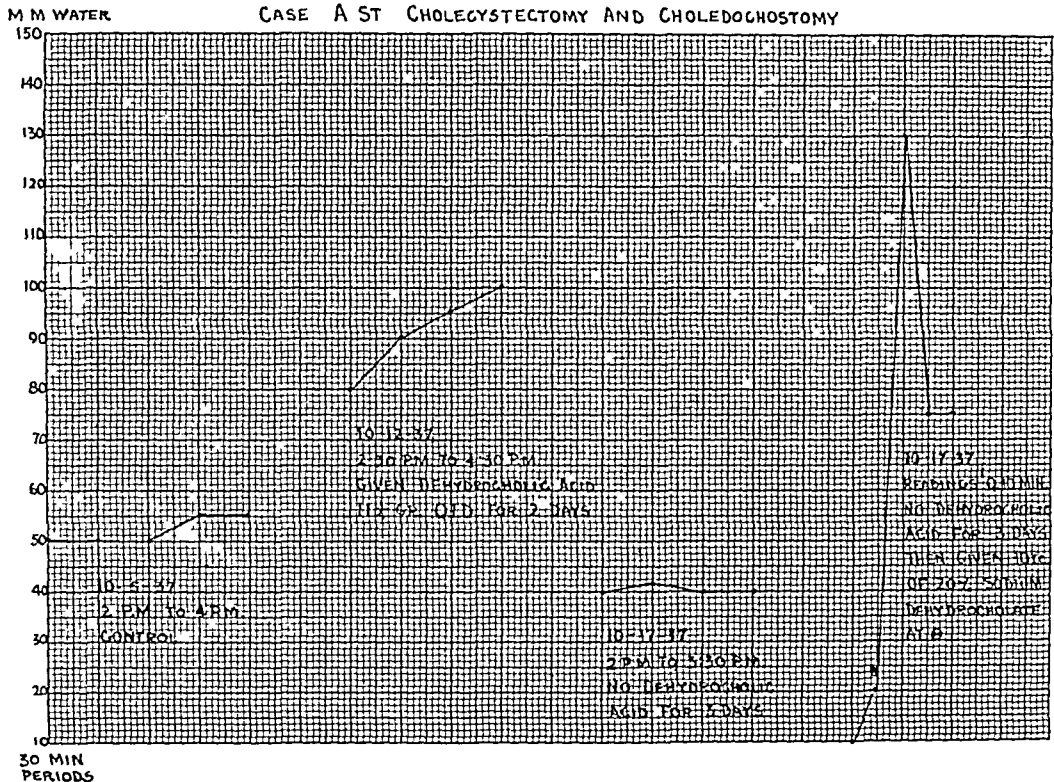


CHART 1—Case 1 A S, female age 58 entered the hospital August 28 1937, complaining of recurrent RU Q pain radiating to the right shoulder blade of 16 years duration. These attacks were associated with rather severe indigestion and vomiting. Nineteen years previous to admission she had had a cholecystostomy after an attack of RU Q pain with jaundice. Graham-Cole studies showed marked impairment of gallbladder function with lithiasis. Cholecystectomy and choledochostomy with T tube in the common duct were performed September 22 1937. The postoperative cholangiogram was negative. Pressure readings were made over a period of three weeks and typical readings are recorded on Chart 1. The control readings varied between 50 and 55 Mm of water. After administration of dehydrocholic acid for several days the level of intraductal pressure was found to vary between 70 and 100 Mm of water. After discontinuing the drug for three days the pressure dropped even to below that of the first control period. Intravenous injection of sodium dehydrocholate resulted in a sudden rise of the pressure to 120 Mm, but this exceedingly high pressure was not sustained.

countered at the point of outlet of the bile, which is the sphincter area. The pressure within the duct will build up with the increase in resistance at the sphincter area. The sphincter "breaking pressure" is that reading where the sphincter gives way to the bile pressure behind it. Various pathologic changes or physiologic disturbances may affect the state of tonus of the sphincter.

Herring and Simpson⁸ also related that the intravenous injection of bile was invariably attended by increased secretion of bile. They found that an increase in biliary pressure followed unless the pressure at the time of injection was high. They concluded, therefore, that a rapid rate of secretion is not essential to the production of a high pressure but that it influences the form of the pressure curve.

BILIARY PRESSURE

Neubauei,¹⁶ in 1923, injected 3 cc of 4 per cent sodium dehydrocholate into the vein of a rabbit and found that the pressure increased nearly 20 Mm within a very few minutes after the injection

Adleisburg and Neubauei,¹ in 1926, attempted to bring about an increased excretion of foreign substance through the liver by means of sodium dehydrocholate They found that no increase occurred in the amount of tetrachlorophenolphthalein excreted by the normal liver or by one whose function was deranged following intravenous administration of sodium dehydrocholate

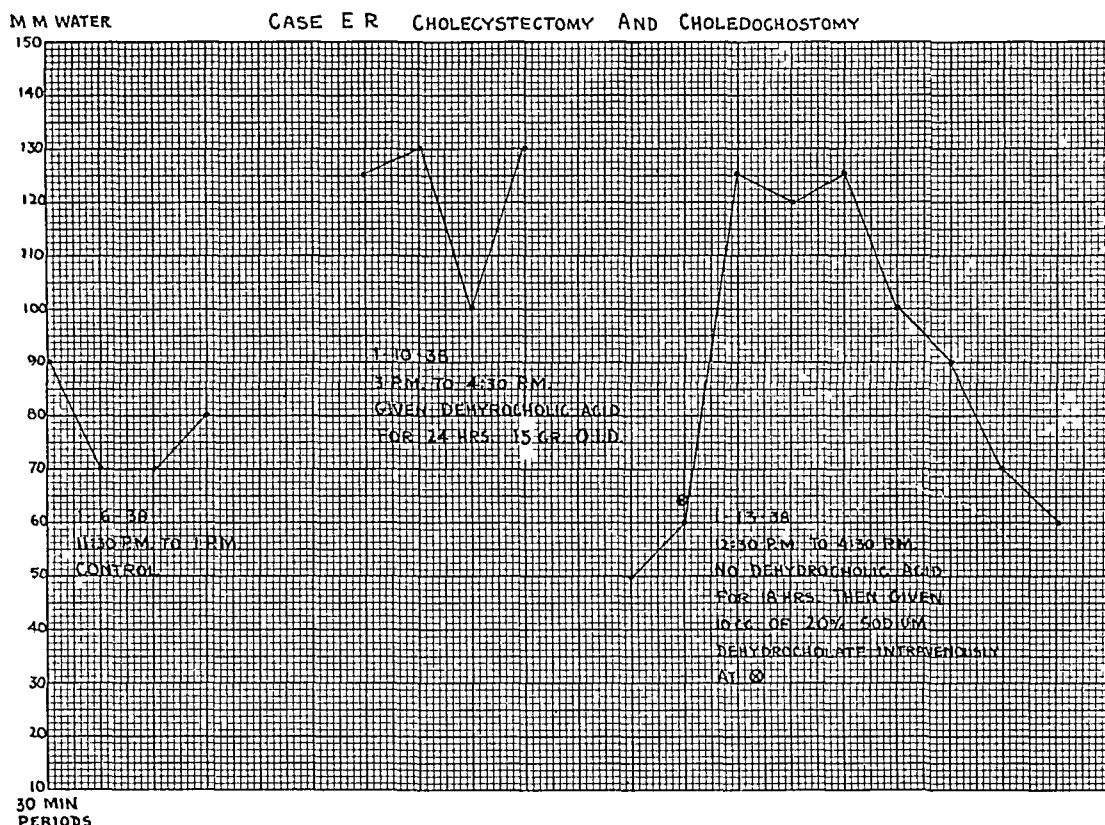


CHART 2—Case 2 E R female, age 22, entered the hospital December 12, 1937, with the history of severe recurrent gallbladder attacks for the past year, requiring hypodermics. No history of jaundice. Physical examination revealed extreme tenderness over the gallbladder. Roentgenograms demonstrated cholelithiasis. Cholecystectomy and choledochostomy were performed December 21, 1937, and three stones were removed from the common duct. A T tube was placed in the duct. The post-operative cholangiogram, on the eighth day, showed a normal duct with no filling defect. Pressure readings were repeated over a period of time and the control readings varied between 70 and 90 Mm of water. Following administration of dehydrocholic acid for 24 hours, the pressure level was considerably higher, varying between 160 and 130 Mm. After discontinuing the dehydrocholic acid for 18 hours, 10 cc of a 20 per cent solution of sodium dehydrocholate were given intravenously. An immediate rise in the pressure to 125 Mm followed, but was not long sustained.

Wakefield, Powelson and McVicar,²² in 1929, found sodium dehydrocholate (decholin) to cause an increased flow of bile in patients who had T-tubes in their common ducts following cholecystectomy. This occurred in 18 out of 20 patients studied. They attributed the increase to a dilution of the constituents normally present.

Sternei, Bartle and Lyon,²¹ in 1931, analyzed somewhat similar studies which they carried out on 21 patients. They found an average bile flow of 80 cc per 10-minute period in the series of control readings taken. After

giving 10 cc of 20 per cent solution of decholin intravenously, there was an increase in this average to 134 cc per 10-minute period

Regan and Hottel,¹⁹ in 1932, demonstrated in dogs that the intravenous injection of 2 Gm of sodium dehydrocholate increased the flow from a biliary fistula within one minute. This effect persisted over periods which varied from two to five hours. By using a common duct manometer, they found that bile pressure was also increased from a previous average of 341 Mm to an average of 385 Mm following the injection.

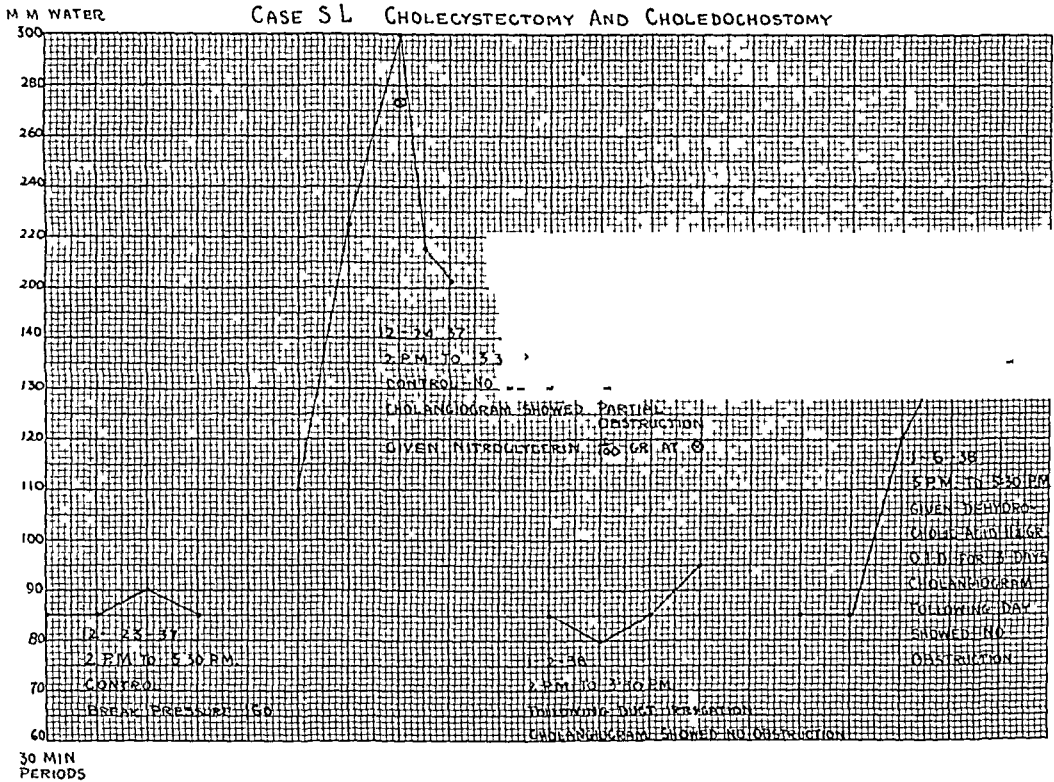


CHART 3—Case 3 S L, female, age 53, entered the hospital with the complaint of recurrent attacks of RUQ pain for the past seven months, one being accompanied by jaundice. She suffered bloating and distress in the epigastrium only with the attacks of pain. Laboratory data were negative except for icteric index of 12. Cholecystectomy and choledochostomy were performed December 15, 1937, and a T tube was placed in the common duct. A cholangiogram December 24, 1937, showed some apparent obstruction in the common duct. The T tube was removed January 10, 1938, and drainage ceased January 13, 1938. The control readings, December 23, 1937, varied between 80 and 90 Mm of water, and the "break" pressure was recorded at 160 Mm. On the following day, another control reading was made, revealing the intraductal pressure to be 300 Mm of water, and as long as the tube was closed off the patient had severe pain in the RUQ, radiating into the back. This was relieved by placing 1/100 Gr of nitroglycerin under the tongue and the pressure dropped to 205 Mm. The common duct was irrigated for several days and by January 2, 1938, the pressure had dropped back to between 80 and 100 Mm. A cholangiogram the following day, showed no obstructing agent. Dehydrocholic acid was then given for three days and intraductal pressure readings rose to between 85 and 140 Mm of water. A cholangiogram, January 7, 1938, again revealed no obstructing agent.

Reinhold and Wilson²⁰ studied the manner in which dehydrocholic acid produced its "striking choleretic action." They concluded that this effect was accomplished primarily by augmented excretion of water, probably associated with rapid excretion of the dehydrocholic acid itself.

Thus, we found a variety of basic experiments which served to guide our study toward dehydrocholic acid and its sodium salt as a choleretic and "choleopressor," in our attempt to evolve a method of increasing biliary pressure in order to flush debris from the common duct.

Technic—Each patient studied in our series was convalescing from cholecystectomy and choledochostomy. At the time of operation a T-tube had been carefully placed into the common duct and brought out through a separate lateral stab wound in every case, and a delayed cholangiogram had been made between the seventh and tenth postoperative days, to investigate the status of the common duct and the sphincter. Most patients were on the general ward diet during the course of the studies but readings were made at the same time of day, insofar as possible.

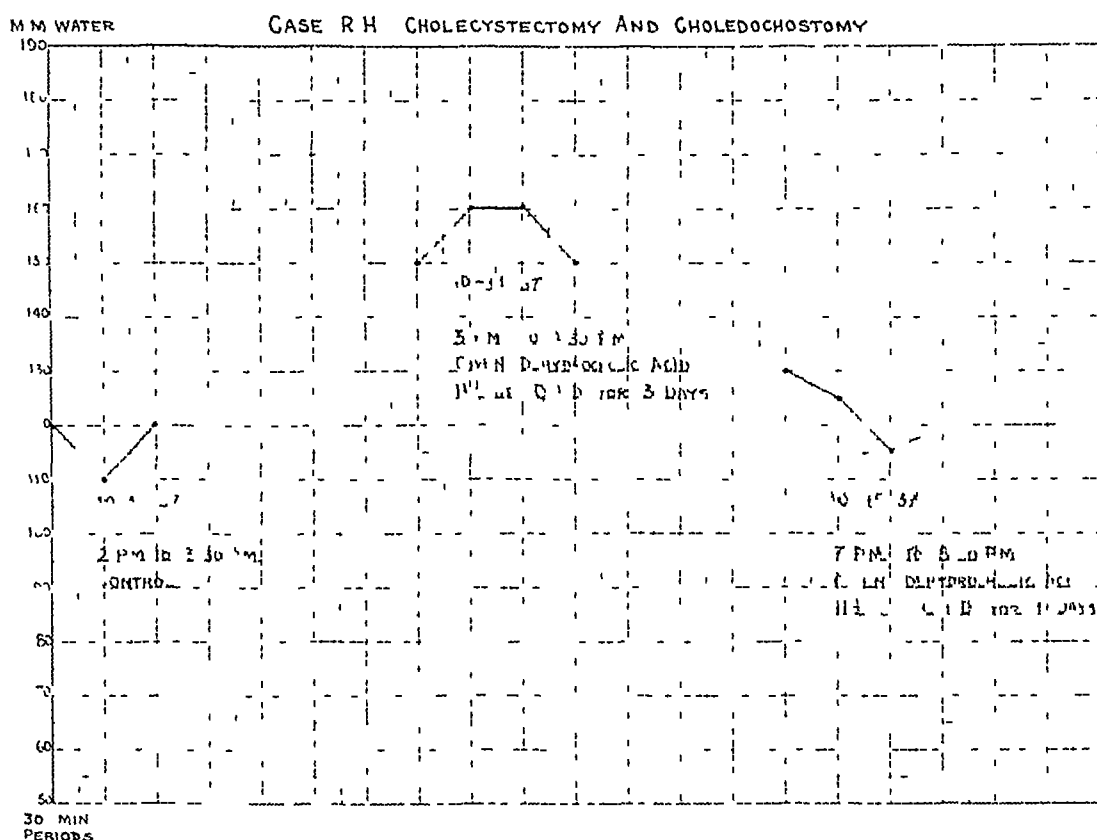


CHART 4—Case 4 R H, female, age 52, was admitted to the hospital September 1, 1937, complaining of recurrent attacks of R U Q pain, radiating to the back over a 10 year period. Late attacks had been associated with chills and followed by fever. She had not been definitely jaundiced but stools were light in color and the urine dark. She had some pruritus, and had indigestion between attacks. The icteric index was 21. Roentgenologic examination did not visualize the gallbladder or calculi. Cholecystectomy and choledochostomy were performed September 22, 1937. Postoperative intraductal pressure readings were taken during a period of eight days and the reading, October 11, 1937, is quite typical of the control readings. On October 14, 1937, it shows the increase in intraductal pressure after administration of 11 1/4 Gr of dehydrocholic acid qid for three days. On the following day, although still on dehydrocholic acid, the general level of the intraductal pressure was lower, but was still a little higher than that during the control period. This drop in the intraductal pressure after three to five days' administration of dehydrocholic acid has occurred rather frequently and is somewhat difficult to interpret, but we are inclined to believe that the increased bile flow may, by increase of pressure, have exhausted the sphincter, or a natural relaxation of the sphincter may follow the administration of this drug over a period of time. The bile output, as we interpret the work of other investigators, does not show a comparative drop.

The manometric equipment consisted of a glass reservoir connected to a glass T-tube, which in turn was connected by one arm to a glass manometer and by the other to a rubber tube which linked the apparatus to the patient's T-tube. The manometer was a straight piece of glass tubing of 2 Mm bore with a centimeter scale beside it (Fig 1).

Before carrying out each experiment, the entire apparatus was sterilized and aseptic technic was carefully followed during the procedure. The reservoir

was filled with sterile normal saline solution warmed to body temperature and the entire system carefully freed of air bubbles. After connecting the apparatus with the patient, the zero point of the manometer was adjusted to the apparent level of the common bile duct. The reservoir was then raised slowly until the solution began to flow freely into the biliary tract and the pressure at this point was noted. This we termed the sphincter "break" pressure. When this reading was determined, the reservoir was lowered until the

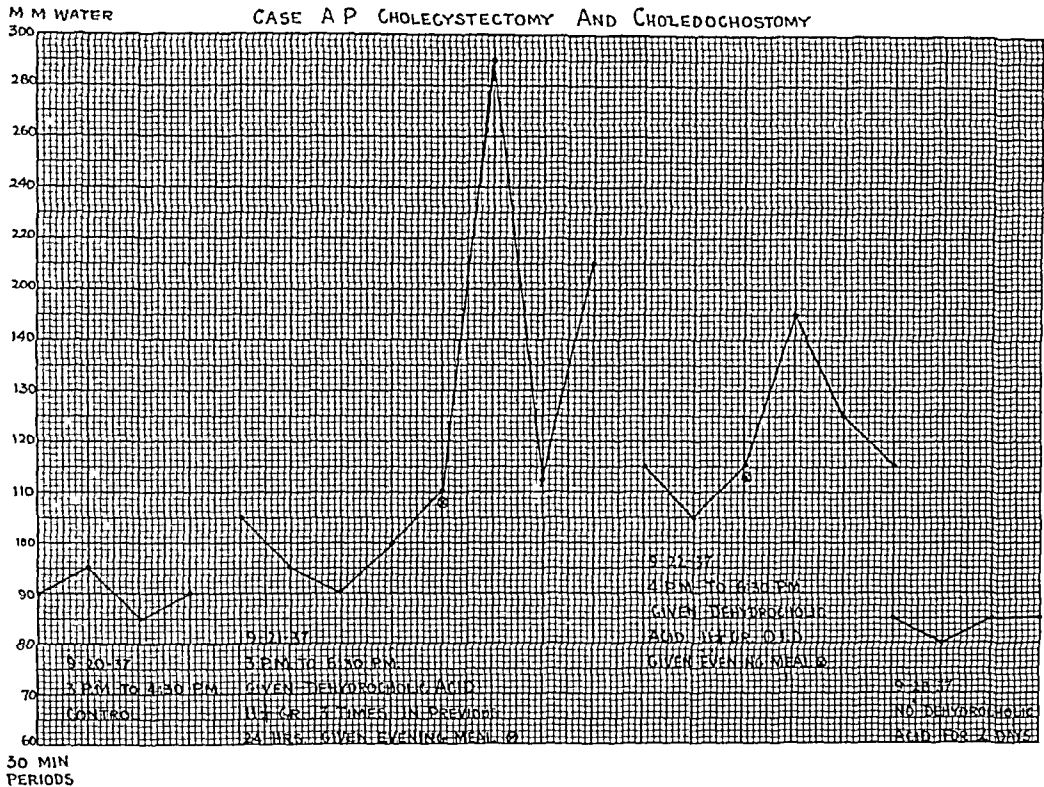


CHART 5—Case 5 A P female, age 58 entered the hospital August 24, 1937, with the history of four attacks of severe RUQ pain, radiating to the back during the last 10 years. These were followed by icterus and pruritus. The last attack occurred one month before admission and was associated with chills, fever, dark urine and clay colored stools. She had been constipated for years. Her icteric index on admission was 9. Cholecystogram revealed faint concentration of dye suggestive of mild cholecystitis. Cholecystectomy and choledochostomy were performed September 4, 1937. A cholangiogram two weeks later showed all ducts clear. The control intraductal pressure readings were taken on several occasions and were found to vary between 80 and 90 Mm of water. The control reading of September 20 1937 is charted. She was given 11 1/4 Gr of dehydrocholic acid t i d, beginning the morning of September 21 1937 and the reading for that afternoon is charted. The general level of intraductal pressure is higher. The evening meal consisting of corn beef hash, cole slaw and chocolate pudding, was served at 5 P M and was followed by an immediate rise in intraductal pressure. This has been interpreted as spasm of the sphincter possibly caused by the rather coarse diet particularly the salad. On September 22 1937, the general level of the pressure is higher and here again a rapid rise occurs at mealtime after the ingestion of scalloped corn, bacon, mixed fruit salad and burnt sugar cake. On September 28 1937 after having had no dehydrocholic acid for two days, we find the intraductal pressure again between 80 and 90 Mm of water. This phenomenon may be the dramatic representation of what occurs in biliary tract disease, and may explain the distress at mealtimes upon the ingestion of certain foods.

manometer read zero and at that point the reservoir was clamped off from the rest of the system. Usually a slow rise of the manometer occurred to indicate the pressure within the ductal system. It is this pressure in which we have been most interested.

All our readings were taken with the patients supine, and the subjects were all sufficiently cooperative to lie quietly during the course of the studies.



FIG 2—(A) In this instance, the biliary fistula would not close and a cholangiogram revealed a filling defect at the lower end of the common duct. (B) After the described treatment, no foreign body was visible on the check up cholangiogram and the fistula closed in three days.

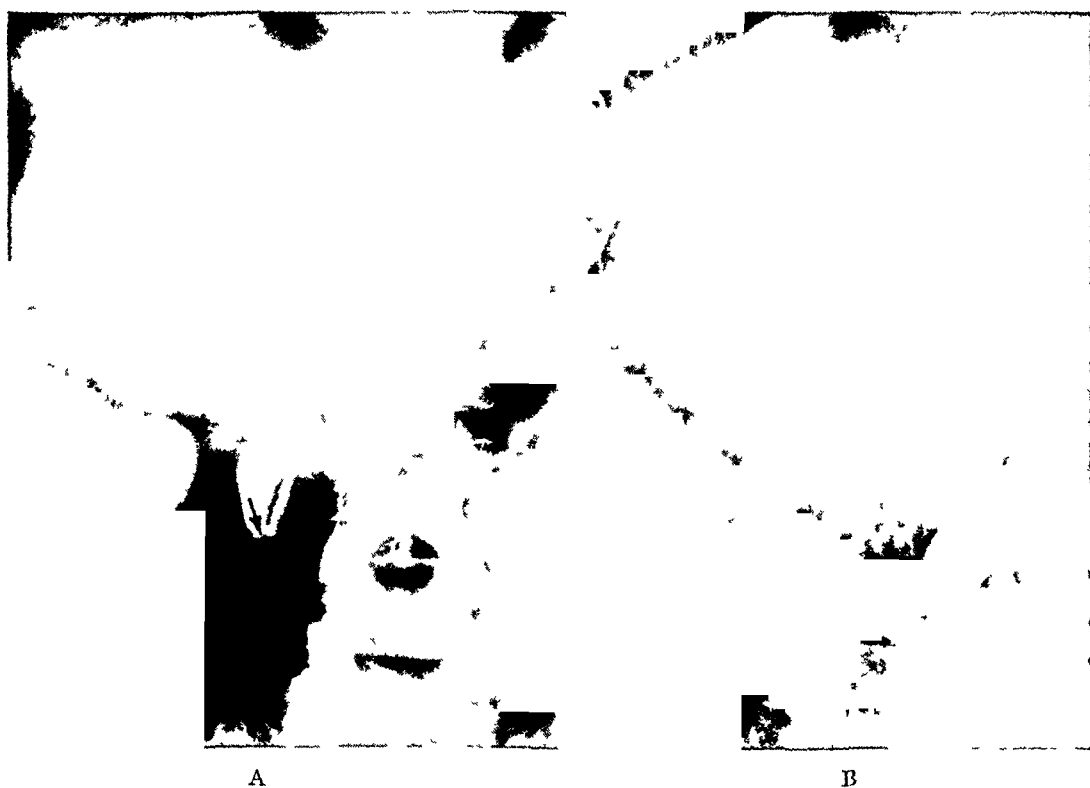


FIG 3—(A) Postoperative cholangiogram revealed a stone remaining in the lower end of the common duct. (B) After several courses of treatment, cholangiogram shows that the stone has been dislodged from the common duct.

Nothing was given by mouth during the time the apparatus was in use except as is indicated in our results. The curves represent the typical readings of a particular patient as recorded over a number of hours on a given day. The water in the manometers would immediately seek a level, which indicated the pressure within the ductal system and which was followed for varying periods of time.

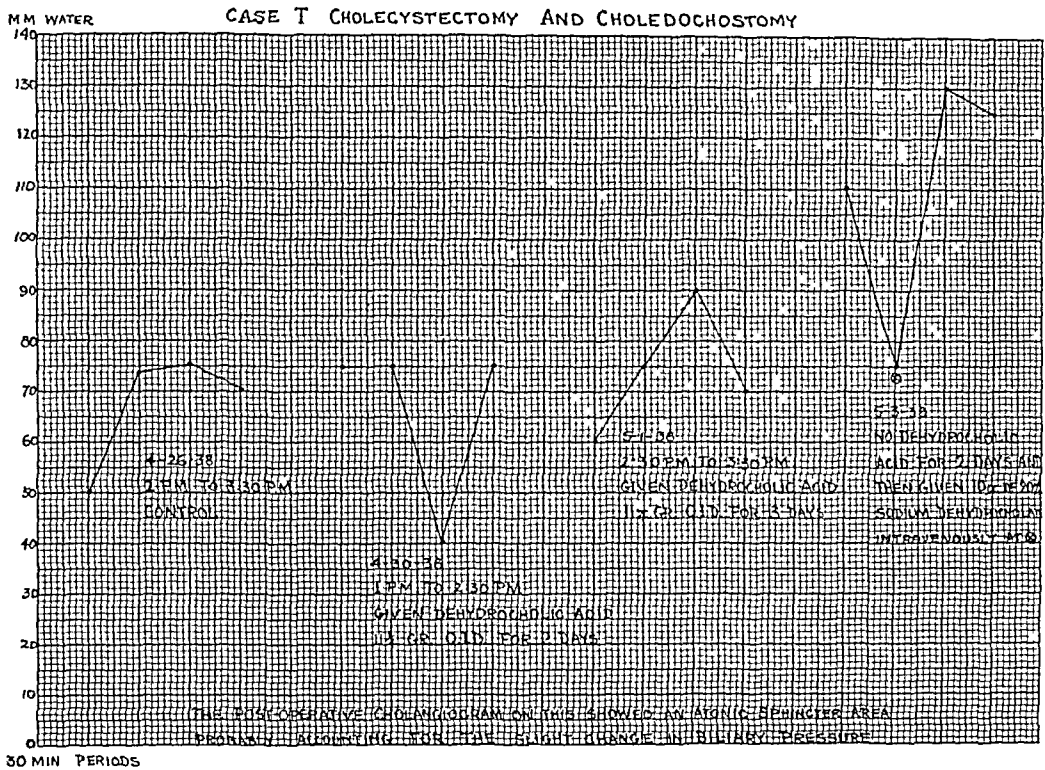


CHART 6—Case 6 Mrs. T, age 40. Although the patient was given dehydrocholic acid, no increase in intraductal pressure occurred. A cholangiogram revealed an atonic sphincter of Oddi, which permitted very free egress of all the contrast medium into the duodenum. After intravenous administration of sodium dehydrocholate, the intraductal pressure increased somewhat.

Interpretation—The accompanying charts reveal the pressure within the common duct following cholecystectomy and choledochostomy. Of course, the pressure might be altered slightly by the presence of the T-tube within the duct, but some unnatural condition is necessary for the recording of the pressure, and all changes may be considered relative. The common duct pressure in the cases reported, as well as in some others not reported in this series, has been found to vary between 50 and 125 Mm. of water. This rather wide variance would seem natural in view of the mechanics and physiology of digestion in different individuals and also at different times in the same individual. The liver secretory pressure, the amount of bile arising at the source in the liver, the inhibitory forces that might be present at the outlet of the bile tubal system, are all factors which will alter the pressure within the duct. Obstructing agents within the duct may cause the pressure to vary as exemplified by Case 3. A choleretic drug, such as decholin or procholol, the commercial products of dehydrocholic acid, may alter conditions at the bile source through stimulation of the secretory cells of the liver, as proved by various investigators previously.

mentioned. The graphs of the five cases presented in this study show that the stimulation is usually accompanied by a definite increase of intraductal pressure, varying between 25 and 75 Mm of water, when the drug is given orally.

We have observed in giving the drug over a period of three to five days, that the intraductal pressure not infrequently returns to a level rather close to the control period. This is illustrated in Case 4, and it may be due to lowering of the "break" pressure at the lower end of the common duct by the unusual intraductal pressure or by direct effect of the drug upon the choledochal

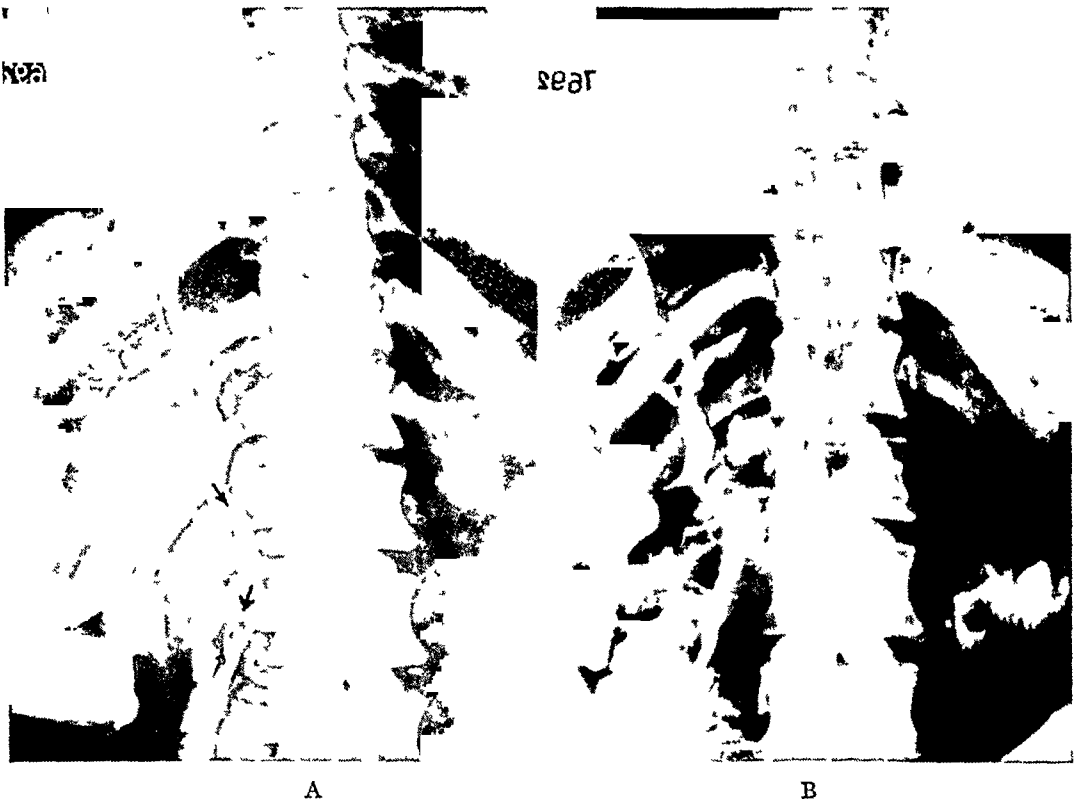


FIG. 4—(A) The postoperative cholangiogram reveals multiple stones in the common duct, although none had been found at operation. These probably came from the higher levels of the hepatic ducts. (B) After two courses of the described treatment, the cholangiogram reveals no remaining stones. Eleven stones were removed from the stools during the period of treatment.

sphincter area. Reference to the investigations of others does not reveal a corresponding drop in the amount of bile fluid at this period. In cases where the dehydrocholic acid is withdrawn for some days and then is administered again, the expected increase in pressure usually occurs, but it usually does not reach the height attained after the first administration of the drug. When the dehydrocholic acid is discontinued, the ductal pressure usually returns to the control level (Cases 1 and 5).

Intravenous administration of the sodium salt of dehydrocholic acid (decholin sodium) results in an immediate increase of the intraductal pressure, usually sustained for only 10 to 30 minutes, after which it drops back to the control level (Cases 1 and 2). However, in most instances it rises 25 to 50 Mm of water higher than when the drug is given by mouth, as exemplified in Case 1. One can well say the rise is sudden and dramatic.

In Case 3, raising of the pressure was brought about by a partial obstruction, probably a mucous plug, at the lower end of the common duct. This was revealed by the cholangiogram and the effect of nitroglycerin in relaxing the sphincter area and partially relieving the obstruction was also well demonstrated.

Our findings do not permit us to agree with Elman and McMaster,^{6, 7} who state that, in general, feeding lowers the resistance to bile flow, which may be interpreted as resulting in a lowered intraductal pressure, as in Case 5 of our series the taking of food resulted in an immediate rise of the intraductal pressure. We also believe that the type of food is most important. A rough diet would probably cause irritation of the sphincter area, while a soft, smooth diet would necessarily be less disturbing. Likewise, a fat reaching this area would probably tend to decrease the pressure by relaxing the sphincter musculature. The time element leads one to believe that the pressure increase following food intake results from closure or tightening of the sphincter area at the lower end of the common duct. However, these authors mention a secondary increase in resistance to bile flow occurring some 20 to 25 minutes after a meal, and since our readings showed that the maximum pressure was attained about 15 minutes after the meal, our findings may be considered similar. This rise in pressure, due apparently to changes in the sphincter area, may be the disturbing phenomenon that gives rise to distress in biliary tract disease, or in the patient from whom the gallbladder has been removed, it may be the cause of the postcholecystectomy syndrome.

Clinical Application—As stated in the introductory paragraph of this paper, our experiences with cholangiography have definitely proved to us that stones are not infrequently left within the common duct or are washed down from the liver into the common duct later, that plugs of mucous or inspissated bile not infrequently inhibit the free flow of bile in the common duct and that even blood clots may be the source of obstruction (Figs. 2, 3 and 4). If these remain within the common duct, biliary symptoms persist or are aggravated and thus account for many of the poor results following cholecystectomies.

In the past, operative intervention was necessary or the patient's distress continued, unless nature expelled the foreign body from the duct. If the patient has a persistent biliary fistula or if a T-tube or catheter has been placed within the common duct, a definite picture of the obstruction may be obtained by injecting 10 to 25 cc. of a sterile contrast medium, such as a 48 per cent solution of hippuran, into the tract or tube. In most cases, we have been able to dislodge these foreign bodies by the following method, unless the obstructing agent was an exceedingly large stone. The pressure within the duct is increased by giving three or four tablets of decholin ($3\frac{3}{4}$ Gm.) or procholon four times a day for three days. On the first day, 1/100 Gm. nitroglycerin is dissolved under the tongue three times during the day, to relax the lower end of the common duct and permit the increased bile flow and pressure to flush out the duct. On the second day, atropine Gm. 1/100 to 1/150, is given by mouth or

hypodermically three times. On the third day, the nitroglycerin is repeated. Each morning before breakfast, during this three-day regimen, the patient is given one to two drams of magnesium sulphate in water and preceding the evening meal and at bedtime, one ounce of pure cream or olive oil, which also aids in relaxing the sphincter area at the lower end of the common duct.

During any momentary relaxation of the sphincter area afforded by these drugs, the increased intraductal pressure may force or flush the foreign body out of the common duct. If a T-tube is present or a biliary fistula exists, the common duct is irrigated each day with sterile, warm normal saline solution followed by sterile, warm olive oil or warm iodized oil such as lipiodol or lipiodine. We now keep the tube clamped or the fistulous tract packed for two to three hours following each administration of the nitroglycerin or atropine. During the night, one may or may not keep the T-tube clamped, depending somewhat upon the degree of obstruction and the amount of pain ensuing. This regimen is now used in all gallbladder cases postoperatively, and since common duct pathology is so common and possibly is the cause of distress in many cases of nonoperative biliary tract disease, it is also used in the medical management of this condition. We have also proved that intrahepatic duct stones may be washed down from the liver by this method. Jaundice with complete obstruction of the common duct definitely contraindicates this method of treatment.

REFERENCES

- ¹ Adlersburg, D., and Neubauer, E. *Über die Beeinflussung von Galle, Blut, und Harn durch Zufuhr von Dehydrocholsäure*. *Ztschr f d ges exper Med*, **48**, 291-305, 1926, as abstracted in *Chem Abst*, **20**, 3039, 1926.
- ² Best, R. R., and Hicken, N. F. *Biliary Dyssynergia*. *Physiological Obstruction of Common Bile Duct*. *Surg, Gynec, and Obst*, **61**, 721-734, 1935.
- ³ Best, R. R., and Hicken, N. F. *Nonoperative Management of Remaining Common Duct Stones*. *J A M A*, **110**, 1257-1261, 1938.
- ⁴ Best, R. R. *Cholangiographic Demonstration of Remaining Common Duct Stone and Its Nonoperative Management*. *Surg, Gynec, and Obst*, **66**, 1040-1046, 1938.
- ⁵ Doubilet, H., and Colp, R. *Resistance of the Sphincter of Oddi in the Human*. *Surg, Gynec, and Obst*, **64**, 622-633, 1937.
- ⁶ Elman, R., and McMaster, P. D. *The Physiological Variations in Resistance to Bile Flow in the Intestines*. *Jour Exper Med*, **44**, 151-172, 1926.
- ⁷ Elman, R., and McMaster, P. D. *On the Expulsion of Bile by the Gallbladder and a Reciprocal Relationship with the Sphincter Activity*. *Jour Exper Med*, **44**, 173-198, 1926.
- ⁸ Herring, P. T., and Simpson, S. *The Pressure of Bile Secretion and the Mechanism of Bile Absorption in Obstruction of the Bile Duct*. *Proc Roy Soc, London, Series B*, **79**, 517-532, 1907.
- ⁹ Judd, E. S., and Mann, F. C. *The Effect of Removal of the Gallbladder and Experimental Study*. *Surg, Gynec, and Obst*, **24**, 437-442, 1917.
- ¹⁰ Koster, H., and Shapiro, A. (Letter) *Variation in Bile Pressure in Human Biliary Tract*. *J A M A*, **107**, 372, 1936.
- ¹¹ Koster, H., Shapiro, A., and Lerner, H. *On the Rate of Secretion of Bile*. *Am Jour Physiol*, **115**, 23-26, 1936.

- ¹² Lueth, H C Studies on the Flow of Bile Into Duodenum and Existence of Sphincter Oddi Am Jour Physiol, 99, 237-252, 1931
- ¹³ Mann, F C A Study of the Tonicity of the Sphincter at the Duodenal End of the Common Bile Duct Jour Lab and Clin Med, 5, 107-110, 1919-20
- ¹⁴ McGowan, J M, Butsch, W L, and Walters, W Pressure in the Common Bile Duct of Man J A M A, 106, 2227-2230, 1936
- ¹⁵ McMaster, P I, Brown, G O, and Rous, P Studies on the Total Bile, on the Bile Changes by a Pressure Obstacle to Secretion, and on Hydrohepatosis Jour Exper Med, 37, 685-698, 1923
- ¹⁶ Neubauer, Ernst Dehydrocholsaure, ein wirksames, praktisch ungiftiges Glied der Gallensauregruppe Klin Wchnschr, 23, 1065-1067, 1923
- ¹⁷ Oddi, R Sul centro spinale dello sfintere de coledoco Sperimentale, 1894, 48, 180, as abstracted in Schmidt's Jahrb, 245, 120, 1895
- ¹⁸ Potter, J C, and Mann, F C Pressure Changes in the Biliary Tract Am Jour Med Sci, 171, 202-217, 1926
- ¹⁹ Regan, J F, and Horrall, O H Physiologic Action of Dehydrocholic Acid Am Jour Physiol, 101, 268-273, 1932
- ²⁰ Reinhold, J G, and Wilson, D W Acid-Base Composition of Hepatic Bile III Effects of Administration of Sodium Cholate and Sodium Dehydrocholate (Decholin) Am Jour Physiol, 107, 400-405, 1934
- ²¹ Sterner, R F, Bartle, H J, and Lyon, B B V The Cholagogue Effect of the Intravenous Injection of Sodium Dehydrocholate, with a Resume of Literature on Bile Salt Metabolism Am Jour Med Sci, 182, 822-839, 1931
- ²² Wakefield, E G, Powelson, H P, and McVicar, C S Use of Sodium Salt of Dehydrocholic Acid (Decholin) as Choleric Ann Int Med, 3, 572-577, 1929

HABITUAL DISLOCATION OF THE DIGITAL EXTENSOR TENDONS

R R FITZGERALD, M D , F R C S (ENG)

MONTREAL, CAN

FROM THE MONTREAL GENERAL HOSPITAL, MONTREAL, CAN

WHEN the fingers are flexed the extensor tendons can be seen to stand out on the rounded heads of the metacarpal bones. Each tendon rests accurately on the apex of the smooth cartilage-covered surface of the bone-end, without any tendency to slide off. The tighter the fist is clenched, the more securely the tendon holds its position. The principal mechanism holding each tendon in place is its adhesion to the capsule of the metacarpophalangeal joint. The intertendinous tissues on the dorsum of the hand also help to hold the tendons in their position, principally through the juncturae tendinum, which are constantly present over the two lateral interosseous spaces, uniting the tendons of the middle, ring, and little fingers. The extensor expansions on the dorsum of each proximal phalanx also assist in keeping each tendon in its proper alignment.

The efficiency of this retaining mechanism is attested by the rarity of reports of habitual displacement. One would expect that pugilists would be likely to suffer from dislocation of tendons on the knuckles, but if such is the case no reports have been placed on record. Krukenberg¹ first wrote of the condition, in 1890. Haberern,² in 1902, gave a description of a case, with an operation for its cure, by constructing a restraining sheath from the subcutaneous tissues and strips of the capsule of the metacarpophalangeal joint. Reports by Paget, Legouest and Howard Marsh were mentioned in this paper. In 1921, Levy⁴ collected six cases from the writings of others, and added four of his own. He recognized pathologic, traumatic, and hereditary types, and approved of the Haberern operation.

Case Report—On September 10, 1936, a young woman, age 22, stenographer, complained that she was unable to use her left hand in operating a typewriter on account of pain in the forearm, associated with slipping of the extensor tendons from the heads of the metacarpal bones whenever the fingertips were pressed on the keys.

Two years previously she had first noticed that the tendon of the index finger slipped off the head of the bone toward the ulnar side whenever the fist was clenched. This sliding of the tendon was always accompanied by an unpleasant sensation passing upward into the forearm. Three weeks before coming for advice, the tendon of the middle finger began to slip in an ulnar direction, and the pain became worse. A fortnight later the tendons of the ring and little fingers became similarly displaced. There was a boring pain, deep in the extensor muscles of the forearm, the hand felt cold, and perspired freely. She obtained relief by allowing the hand to hang loosely by the side. No relative of the patient had ever suffered from a similar condition.

Physical Examination—There was slight wasting ($\frac{1}{2}$ cm in circumference) in the arm and forearm. There was no displacement of the tendons when the interphalangeal joints were flexed with the metacarpophalangeal joints extended, neither was there any slipping when the metacarpophalangeal joints were flexed while the interphalangeal

were kept straight. But when all three joints were flexed the tendons slid off the heads of the bones with a visible jerk, associated with an irritating sensation of deep soreness in the forearm.

The tendons of the index, middle, and little fingers always went to the ulnar side, that of the ring finger to the radial side of the corresponding bone (Fig 1). The tendons slid abruptly back into position as soon as extension was begun.

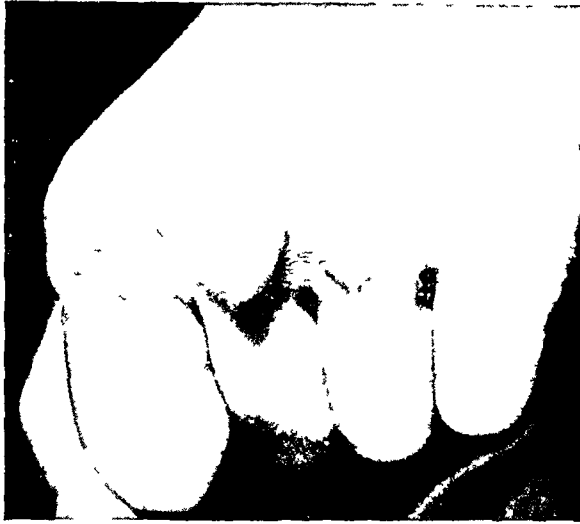


FIG 1—Before operation. The tendons of the index, middle, and little fingers are displaced toward the ulnar side of the head of the corresponding metacarpal. That of the ring finger has slid off in a radial direction. Pain was felt in the forearm.

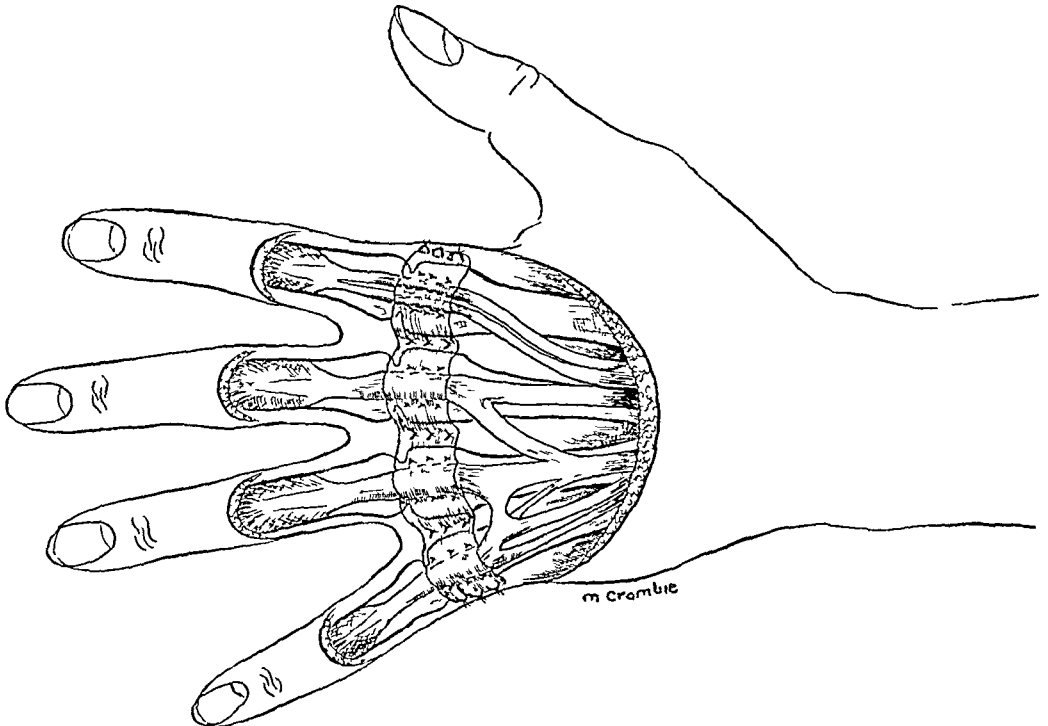


FIG 2—Method of fixing the fascial strip in position. Note that the common extensor expansions are absent over the upper part of the proximal phalanx.

Operation—September 29, 1936. Under general anesthesia, a strip of fascia lata 12 cm long and $\frac{1}{2}$ cm wide was removed from the outer side of the right thigh. Three longitudinal incisions were then made over the interosseous spaces and continued distally along the dorsum of the index, ring, and little fingers. The extensor

tendons had a normal attachment to the fibrous capsule of the joint. *Juncturae tendinum* were seen to be present. The common extensor aponeurosis, however, did not appear to extend as far proximally as usual. In a normal hand the proximal edge of the extensor expansion is situated at the metacarpophalangeal joint line, and in fact, in hyperextension it slips over a part of the metacarpal head and partly covers its articular

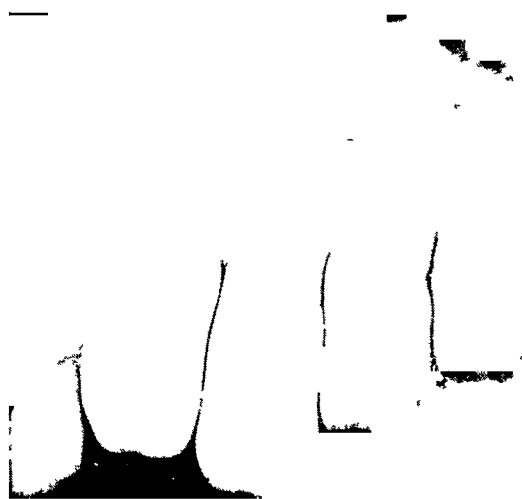


FIG. 3—Two months after operation. The scars are visible, and the tendons remain in place on flexion. No pain. (The ridge on the radial side of the head of the index metacarpal is due to a distended vein.)

surface. In some dissections it blends with the capsule of the metacarpophalangeal joint. Apparently, in the instance here described, it was the absence of this usually well developed proximal part of the common extensor aponeurosis that permitted the tendons to slide off the smooth heads of the bones during flexion of the digits.

The strip of fascia lata was anchored to the periosteum on the radial side of the head of the index metacarpal with silk sutures. It was also anchored to the transverse ligament of the heads of the bones between each pair of metacarpals, and to the periosteum on the ulnar side of the fifth metacarpal. Fine sutures were then placed along both sides of each tendon, anchoring the strip of fascia lata down to the joint capsule. At the close of the operation each tendon was held down to the fibrous joint capsule in a tunnel of fascia lata, which in turn was fastened to each side of the deeper tissues (Fig. 2). The skin was closed with fine silk sutures. The wounds healed by primary union, and exercises were begun in ten days (Fig. 3).

Follow-Up—On November 20, 1936, the patient returned to her work as a stenographer, and ever since that date she has been able to type at the same speed as before. The pain has completely disappeared. The tendons remain in place on all movements. The range of movement of the metacarpophalangeal joints is two-thirds that of normal, that of the interphalangeal joints is normal.

SUMMARY

In a patient with habitual dislocation of the digital extensor tendons, dissection at operation showed that the proximal edge of each common extensor expansion was placed a little further distally on the proximal phalanx than is usually the case. This anatomic fact is offered as an explanation of the dislocation. An operation for the cure of the condition is described.

REFERENCES

- ¹Krukenberg. *Jahrb. d. Hamburg Krank.*, 2, 232, 1890.
- ²Haberern, J. P. *Deutsche Zeitschr. f. Chir.*, 62, 191, 1902.
- ³Spitzzy. *Archiv f. Orthopadie*, 1, 1903.
- ⁴Levy, W. *Zentralbl. f. Chir.*, 48, 482, 1921.

STUDIES OF CYCLOPROPANE THE USE OF BARBITURATES IN PREVENTING CARDIAC IRREGULARITIES UNDER CYCLOPROPANE OR MORPHINE AND CYCLOPROPANE ANESTHESIA

AN EXPERIMENTAL STUDY

BENJAMIN H. ROBBINS, M.D., JAMES H. BAXTER, JR., B.S., AND
O. GARTH FITZHUGH, PH.D.

NASHVILLE, TENN.

FROM THE DEPARTMENT OF PHARMACOLOGY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

PATIENTS anesthetized with cyclopropane, after the usual premedication with morphine and atropine, frequently develop cardiac irregularities during some stage of the anesthesia. In the course of an experimental investigation, it was found that in dogs anesthetized with cyclopropane alone, cardiac irregularities were very rarely encountered until after respiratory arrest, whereas, in those medicated with morphine and anesthetized with cyclopropane, cardiac irregularities were present in practically all cases during some stage of anesthesia. Dogs that are given barbiturates as preanesthetic medication do not develop cardiac irregularities with cyclopropane during surgical anesthesia and only rarely after respiratory arrest.

Lucas and Henderson¹ were the first to observe occasional irregularities of the heart in animals under cyclopropane anesthesia. Kurtz, Bennett and Shapiro,² in an electrocardiographic study, found ventricular extrasystoles in over one-half and multiple focus ventricular tachycardia in 10 per cent of their patients anesthetized with cyclopropane.

SeEVERS, *et al.*,³ in a study on dogs under cyclopropane anesthesia, found that cardiac irregularities came on at the time of, or soon after, respiratory arrest, and that normal rhythm would return immediately upon giving artificial respiration or reducing the concentration of cyclopropane in the bag by diluting with oxygen. They also found that atropine would abolish the initial irregularities and state that these are probably of vagal origin. Robbins and Baxter⁴ reported a study similar to that of SeEVERS, *et al.*, except that they made analyses of the blood for oxygen, carbon dioxide, and cyclopropane, and found that the electrocardiographic changes were always associated—except in one of 13 dogs—with severe anoxemia, and that with adequate artificial respiration the heart remained normal with a much higher concentration of cyclopropane in the blood than that necessary to produce respiratory arrest. In a study analyzing the effect of cyclopropane upon the different properties of the heart, Meek, Hathaway, and Oith⁵ have shown that the heart of a dog anesthetized with cyclopropane is more sensitive to an injection of a small amount of epinephrine than the heart of a normal dog or of one under chloro-

form of ether, and state that cyclopropane increases the irritability of the automatic tissues of the heart more than these other agents

Many investigators⁶ have reported that certain barbiturates reduced or abolished the effect of vagal stimulation upon the heart, in a recent paper by Gruber, *et al*,⁶ a review of this subject is presented. Seevers and Meek,⁷ and Hoff and Nahum⁸ showed that some of the barbiturates prevented the development of cardiac irregularities following the intravenous injection of ephedrine or calcium chloride, which increase the irritability of the heart

The effect of morphine upon the rate and rhythm of the heart has been studied by many investigators, and all are agreed that the bradycardia and arrhythmia result from excessive vagal tone. Jackson and Ewing⁹ found that morphine reduces the threshold for the vagal reflexes, McCrea and Meek¹⁰ believe that the primary site of action of morphine in producing the changes in heart rate and rhythm is in the cerebrum, but more recent studies by Robbins, Fitzhugh and Baxter¹¹ show that the typical morphine bradycardia persists after decerebration of the dog

Cyclopropane anesthesia intensifies the bradycardia and arrhythmia in dogs medicated with morphine, an analysis of this action, which will be published elsewhere,¹² showed that cyclopropane increased the action of morphine through the vagal system

With evidence that barbiturates depress vagal tone and decrease the irritability of the automatic tissues of the heart and that the irregularities under morphine and cyclopropane anesthesia are due in part to vagal action and increased irritability of the automatic tissues, we decided to follow up our earlier observations of barbiturate-cyclopropane and morphine-cyclopropane action on the heart

METHODS—*Electrocardiographic Study* A standard Cambridge electrocardiograph was used. The records were taken from Lead II and were analyzed for rate, P-R interval, and T-wave changes, as well as for abnormalities

Blood Gases The Van Slyke-Neill manometric apparatus was used for the oxygen and carbon dioxide analyses. Arterial blood was collected under oil and one cubic centimeter samples were analyzed, duplicate analyses were not made routinely. The cyclopropane content of the blood was determined on five cubic centimeter samples by the iodine pentoxide oxidation method as described in an earlier paper.¹³

Preparation of the Anesthetics and Mode of Administration Morphine sulphate was given subcutaneously, barbitol or amytal was used in a 10 per cent solution and was injected into the great saphenous vein in the amounts recorded in the tables. Thirty minutes after the injection of the preanesthetic drug, anesthesia was completed by having the dog rebreathe in a bag containing a mixture of cyclopropane and oxygen. As soon as anesthesia was sufficiently deep to permit, a tracheal catheter with an inflatable cuff was inserted and then connected in line with the soda-lime filter and bag containing the anesthetic mixture. The bag was emptied and refilled two or three times dur-

ing each experiment in order to remove the inert gas. Oxygen was added continuously at the rate of its consumption.

Animal Experiments The dog was placed, back down, on a dog board, and connections were made for taking electrocardiographic records. After the control record was made, the right hind leg was shaved for the intravenous injection of the barbiturate. The barbiturate was injected over a period of one or two minutes. Thirty minutes after the injection of the barbiturate or morphine, a second electrocardiographic record was made, and then the anesthesia was completed by giving cyclopropane in oxygen. The dog was kept in deep surgical anesthesia for 30 minutes, and then arterial blood samples were drawn for oxygen, carbon dioxide, and cyclopropane analyses, an electrocardiographic record was made. The image of the string was under constant observation from the time of administration of cyclopropane.

TABLE I

Exper No	—Premedication— Type Amount		Arterial Gases								Interval Between Respiratory Ar rest and Cardiac Arrest Minutes	Remarks
			Surgical		Respiratory			Cardiac				
			Anesthesia		Arrest			Arrest				
	O	CO	O	CO	C ₃ H ₆	O	CO					
		Mg /Kg	Per Cent	Per Cent	Per Cent	Per Cent	M+	Per Cent	Per Cent			
1	Barbital	250*	14.5	57.0	18.8	65.0	23.1	3.9	78.0	31	No irregularities	
2	Barbital	250			21.0	51.0	25.9	4.3	79.0	42	No irregularities	
3	Barbital	250			17.6	53.5	25.8	2.4	60.0	10	No irregularities	
4	Barbital	250	16.8	45.5	18.6	59.0	23.2	1.9	63.0	8	Two ventricular ex trasystoles before arrest	
5	Barbital	250	21.8	53.5	22.9	67.5	26.0	5.3	77.0	20	Slowing to arrest	
6	Barbital	250			25.0	61.0	27.6	4.1	64.0	8	Slowing to arrest	
AV	Barbital	250	17.7	52.0	20.65	59.2	24.6	3.6	70.1	20		
14	Barbital	150	19.1	44.8	23.5	58.0	26.8	2.3	74.8	18	Slowing to arrest	
15	Barbital	100	18.1	49.5	17.9	63.2	31.0	2.2	70.5	7	AV block, nodal	
7	Amytal	30	18.5	48.5	18.0	62.0	26.1	4.1	69.7	14	No irregularities	
9	Amytal	30	17.0	43.5	21.0	55.4	26.8	2.8	66.7	30	Slowing to arrest	
10	Amytal	30	19.3	47.8	23.4	61.0	34.7	3.1	72.0	18	Slowing to arrest	
11	Amytal	30	16.4	47.4	20.2	59.6	34.6	2.6	70.6	23	Slowing to arrest	
12	Amytal	30	17.5	44.3	19.2	55.5	26.8	3.6	65.7	12	Slowing to arrest	
13	Amytal	30	18.0	45.2	20.8	55.4	34.6	3.5	69.5	17	Slowing to arrest	
AV	Amytal	30	17.8	46.1	20.4	59.1	30.6	3.3	69.0	19		
19 AV	Control	—	18.95	42.7	15.4	51.2	32.7	2.25	55.6	6.2	Nodal rhythm, 16 dogs; AV block, 6 dogs; V ex., 5 dogs	

* The large doses of barbital and amytal reported in this table were used to see if one could prevent the development of cardiac irregularities which are observed in dogs after respiratory arrest, produced by cyclopropane when the arterial oxygen content has been reduced to 3 to 4 volumes per cent. Severe anoxemia alone will cause irregularities of the type shown in Figure 3.

The concentration of cyclopropane in the inspired cyclopropane-oxygen mixture was gradually increased until respiration stopped. Blood samples were then collected for analysis, and an electrocardiographic record was made. During the interval between respiratory arrest and cardiac arrest, which varied from seven to 42 minutes in the dogs given barbiturates, frequent electrocardiographic records were made, and blood samples were collected every five minutes for gas analysis. Immediately after cardiac arrest, final blood samples

BARBITURATES WITH CYCLOPROPANE

were collected By following the change in pulse rate and pressure manually, as well as by watching the image of the electrocardiographic string, we were able, in a majority of the experiments, to predict the time of cardiac arrest, so that the final record showed the complexes just prior to arrest

In this study, eight dogs were given barbitol in doses of 100 to 250 mg per kg, and six were given amytal in 30 mg per kg doses Six dogs were given morphine sulfate in 5 mg per kg doses

TABLE II

EXPERIMENT NO 19 DOG, 9.7 KG, MALE

Time	Stage	Arterial			EKG Number	Heart Rate	P-R Interval	T-Wave	Rhythm
		CO ₂ Per Cent	O ₂ Per Cent	C ₃ H ₆ Mg					
1 10	Control	41.0	15.7	—	1	140	1	+	Slight sinus arrhythmia
1 15	Morphine	—	—	—	—	—	—	—	—
1 45	—	42.6	16.0	—	2	70	1	+	Marked sinus arrhythmia
1 50	C ₃ H ₆ on	—	—	—	—	—	—	—	—
1 52	—	—	—	—	4	52	12	+	Sinus arrhythmia, nodal extrasystoles
1 58	III ₂	—	—	—	5	48	11	—	Nodal and ventricular extrasystoles
2 05	III ₂	45.2	17.5	17.6	6	48	11	+	Ventricular extrasystoles
2 15	III ₂₋₄	—	—	—	7	50	10-12	+	Ventricular extrasystoles
2 25	III ₄	46.8	16.1	23.4	8	46	12	+	Ventricular extrasystoles
2 50	IV	57.2	16.2	27.0	12	62	12	+	Slight sinus arrhythmia
2 51	C ₃ H ₆ off	—	—	—	—	—	—	—	—
	Recovery								

TABLE III

EXPLRIMENT NO 13 DOG, 11.6 KG, FEMALE

Time	Stage	Arterial			EKG Number	Heart Rate	P-R Interval	T-Wave	Rhythm
		CO Per Cent	O ₂ Per Cent	C ₃ H ₆ Mg					
8 55					1	150	10	—	Sinus arrhythmia
9 00	Amytal 30 mg/Kg								
9 20	I				2	140	08	—	Regular
9 25	C ₃ H ₆ on								
10 00	III ₁	45.2	18.0	10.4	3	175	07	—	Regular
11 00	IV	55.4	20.8	31.0	5	220	07	—	Regular
11 05	IV	63.5	18.95		6	250	07	—	Regular
11 10	IV	65.5	15.7		8	210	08	—	Regular
11 15	IV	67.8	8.4		10	175	08	—	Regular
11 17.5		62.5	3.58	34.6	12	40-0	10	—	Slowing to arrest

The results of this investigation are shown in Table I, in which are recorded the type and amount of premedication, the arterial oxygen and carbon dioxide content in surgical anesthesia, at respiratory arrest, and at the time of cardiac arrest, the concentration of cyclopropane in the blood at the time of respiratory arrest, and finally remarks as to the type of cardiac arrest The data in the bottom line are taken in part from an earlier paper⁴ with the addition of results from six other experiments

Protocols of two experiments are given in Tables II and III, electrocardiographic records from these two experiments are shown in Figures 1 and 2

The first abnormal electrocardiographic record from each of five non-premedicated dogs is shown in Figure 3. These irregularities developed on an average of 43 minutes after respiratory arrest produced by cyclopropane alone, the arterial oxygen content was 39 volumes per cent at the time these records were made.

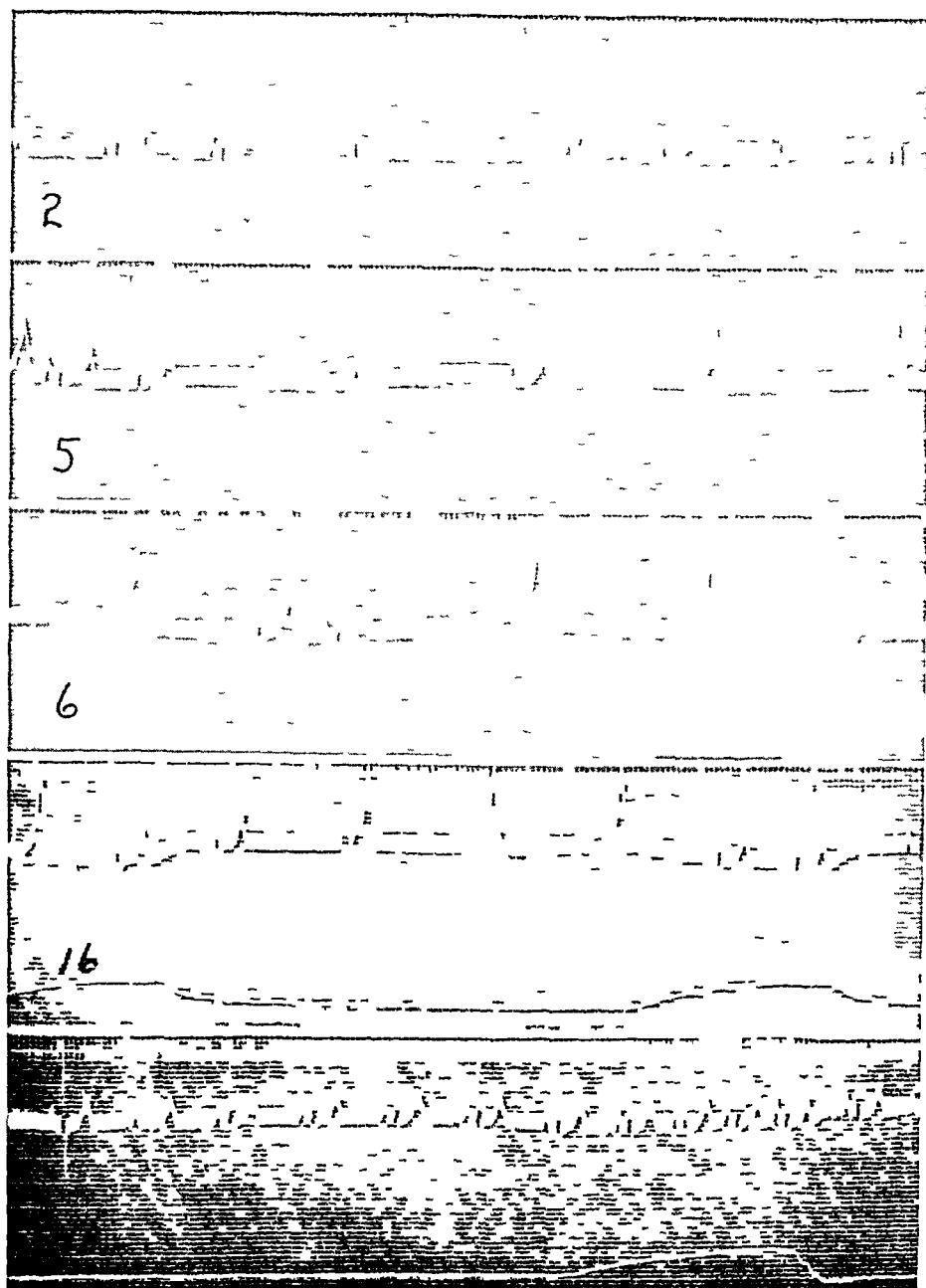


FIG 1—Electrocardiographic Records from Experiment 19. Morphine, 5 mg per Kg, was given as a preanesthetic drug.

Consult Table II for data which correlate the stage of anesthesia, arterial concentration of oxygen, carbon dioxide, and cyclopropane with the first three records in this figure.

The irregularities of the heart in dogs under morphine cyclopropane anesthesia are due to excessive vagal tone. In records 16 and 18 the respiratory activity is correlated with the heart record. The physiologic depression of the vagus center during inspiration permits the heart to beat normally, as shown in record 16. Two minutes after record 16 was made, the dog was given 10 mg per Kg of amytal intravenously, three minutes later record 18 was made. This shows that amytal abolishes the excessive vagal tone.

Discussion—In the dogs receiving morphine, the heart rate fell from a control of 134 to 73, only one dog showed abnormal rhythm before cyclopropane. Anesthesia produced with cyclopropane reduced the rate to 54 per

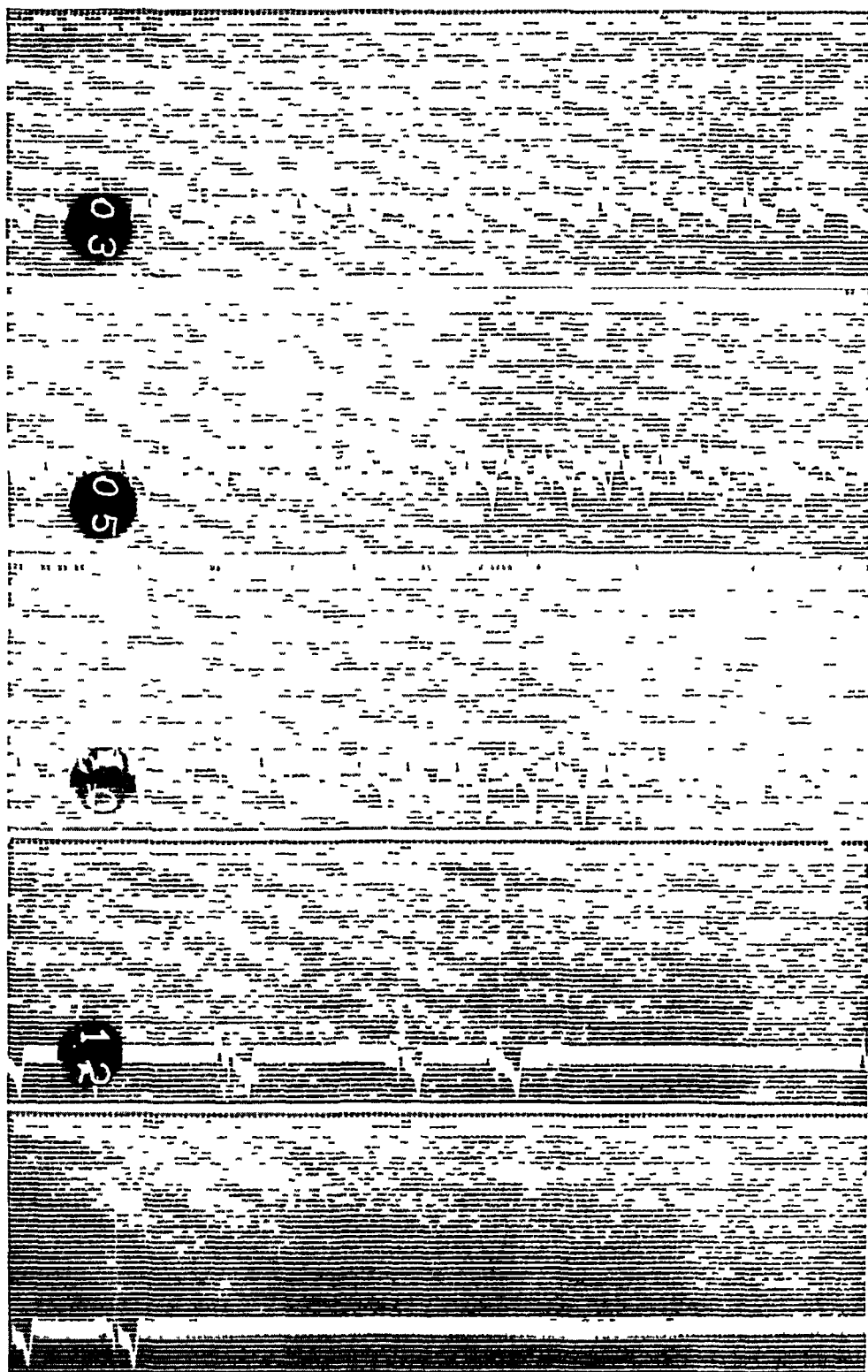


FIG 2—Electrocardiographic Records from Experiment 13, Amytal 30 mg per Kg was given as a preanesthetic drug. Consult Table III, for data which correlate the stage of anesthesia, arterial concentration of oxygen, carbon dioxide, and cyclopropane with the records in this figure. The heart stopped 17.5 minutes after respiratory arrest, as shown in record 12, the arterial oxygen content was 3.58 volumes per cent.

minute, and all dogs showed either nodal or ventricular extrasystoles, even though the arterial oxygen was 17.4 volumes per cent. These results are markedly different from those obtained from dogs receiving cyclopropane alone and from dogs receiving barbiturates before the cyclopropane.

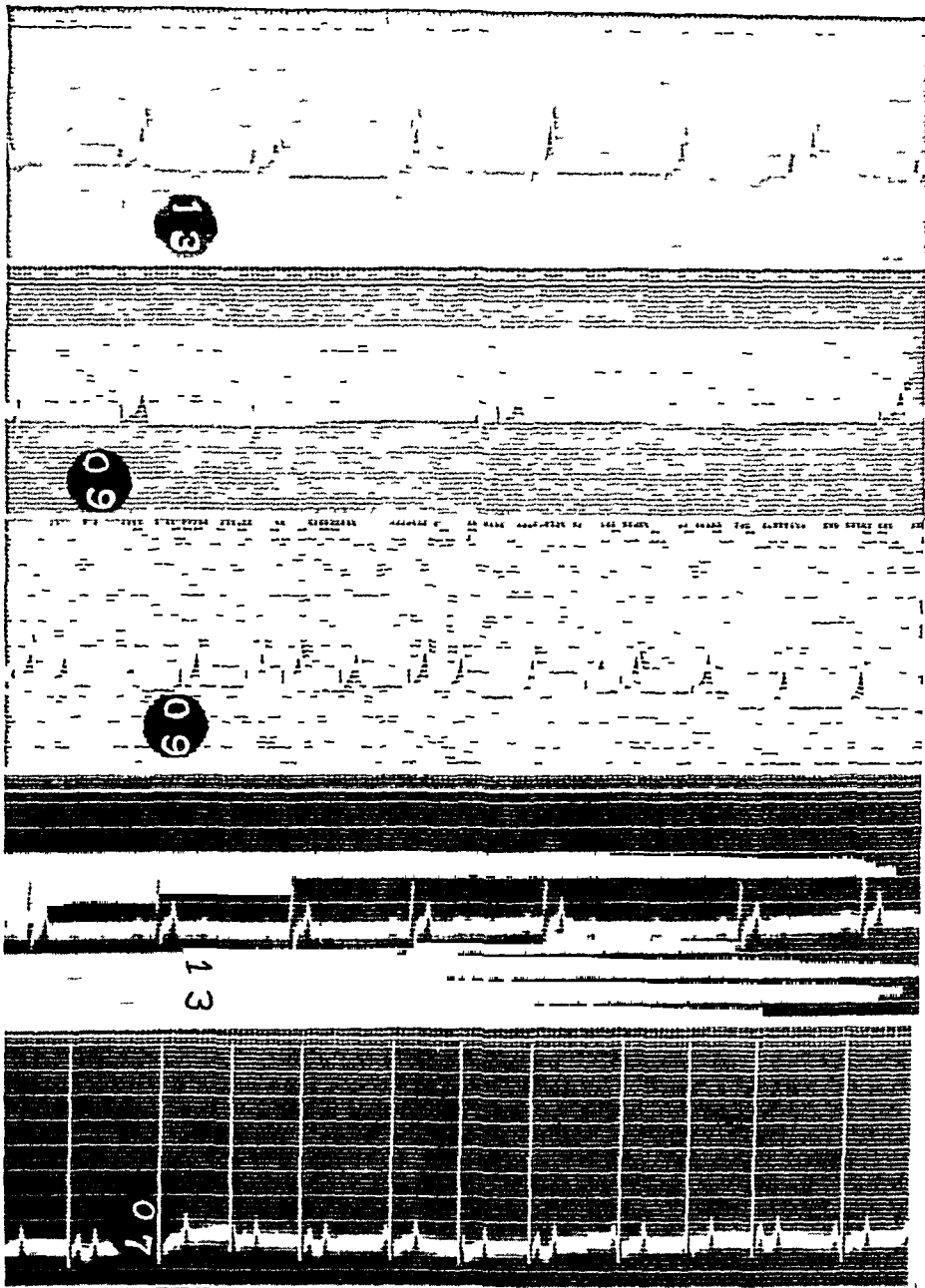


FIG. 3—Electrocardiographic Records from Five Dogs Which Received No Pre anesthetic Medication. The dogs were forced to respiratory arrest by gradually increasing the cyclopropane content of the anesthetic mixture. There were no cardiac irregularities present before respiratory arrest. The irregularities shown above developed 4.3 minutes after respiratory arrest and with an arterial oxygen concentration of 3.9 volumes per cent.

- 13—Ventricular extrasystole arising from a single focus
- 09—Complete auriculoventricular dissociation with slow rate, auricles 32/1', ventricles 20/1'
- 09—Tachycardia of nodal origin, 140/1'
- 13—Partial AV block 2:1 to 3:1
- 07—Auriculoventricular dissociation—auricles regular 100/1', ventricles irregular 100/1'. The shadow of the upstroke of R has been intensified.

The records from the dogs receiving barbiturates show some things in common with the records of the nonpremedicated control dogs. The arterial oxygen concentrations at which arrhythmias or arrest occurred are approximately the same in each group. The concentration of cyclopropane in the blood of the dogs receiving the smaller doses of barbital and in all those receiving amytal is of the same order of magnitude as the concentration in the control dogs, so that the difference in the cardiac picture cannot be ascribed to a difference in the cyclopropane content.

There are three significant differences between the control group and the barbiturate-premedicated groups. First, cardiac irregularities or arrest developed in the control dogs on an average of six minutes after respiratory arrest, whereas, in the barbital- and amytal-treated groups the cardiac arrest occurred about 20 minutes after respiratory arrest. Second, cardiac irregularities were recorded in 17 of the 19 control dogs (16, nodal rhythm, five, auriculo-ventricular block, six, ventricular extrasystole), whereas, in the 14 dogs receiving barbiturates, irregularities were observed and recorded in only two dogs. This is particularly significant when one considers that in the group of dogs receiving amytal, in which the cyclopropane concentration was equal to that in the controls, the final electrocardiographic records show normal complexes even up to cardiac arrest. Third, the arterial content of oxygen is increased at the time of respiratory arrest in the premedicated dogs. In the control group, the oxygen content in surgical anesthesia was 18.95 volumes per cent and at respiratory arrest was 15.40 volumes per cent, whereas, in the amytal group the values were 17.8 and 20.4 volumes per cent, respectively, and in the barbital group the concentration at respiratory arrest was 20.5 volumes per cent. In three dogs receiving barbiturate-premedication the oxygen capacity of the arterial blood in surgical anesthesia and at respiratory arrest was found to be 17.8 volumes per cent and 19.9 volumes per cent, respectively.

Dogs anesthetized with cyclopropane to the stage of respiratory arrest are easily revived by discontinuing the anesthetic and giving artificial respiration for a few seconds. In a group of dogs which received barbiturate-premedication and were forced to respiratory arrest with cyclopropane, several were revived five to 35 minutes after respiratory arrest.

We believe that these results may warrant the trial of a barbiturate in place of morphine as a preanesthetic drug with cyclopropane, until further studies on other barbiturates are completed, amytal is suggested for this use. This suggestion is based on several considerations. The general reports from anesthetists are that the cardiac irregularities observed with cyclopropane are of two types. First, a bradycardia with ventricular extrasystoles—due probably to excessive vagal tone. Second, a tachycardia of nodal or ventricular origin that may be explained on an increased irritability of the automatic tissues of the heart, as reported by Meek, Hathaway, and Oith⁵. In the experiments reported, we have shown that morphine and cyclopropane combined produced a marked bradycardia and irregularities in dogs in surgical anes-

thesia even in the presence of adequate arterial oxygen, and that amytal, in one-half the anesthetic dose, prevented the development of cardiac irregularities in the presence of high cyclopropane concentration in the arterial blood and severe anoxemia. We feel that amytal reduces the excessive vagal tone which is present with morphine and cyclopropane anesthesia and also that the increased irritability of the myocardium and automatic tissues, due to cyclopropane and anoxemia, is reduced to a level below the irritability of the sino-auricular node.

There is little reason to believe that the combination of amytal and cyclopropane will depress the respiration to such an extent that anoxemia will result before respiratory arrest, because blood gas analysis shows adequate oxygen not only at the time of but even for several minutes after respiratory arrest.

The amount of amytal found to be effective in abolishing the cardiac irregularities routinely observed during surgical anesthesia in dogs premedicated with morphine and anesthetized with cyclopropane, could be used clinically. A dose of amytal, 10 mg per Kg, which will abolish the morphine-cyclopropane irregularities in dog is equal to 20 per cent of the anesthetic dose, by analogy an equivalent amount for man would be 4 to 5 mg per Kg, or 280 to 350 mg for the average adult. This amount of amytal would not be considered excessive premedication in the absence of morphine.

It remains for the clinical anesthetist to determine if such premedication will reduce the frequency of cardiac irregularities in man during anesthesia with cyclopropane.

SUMMARY

(1) In a series of 20 dogs receiving morphine, barbital, or amytal as premedication agents for cyclopropane anesthesia, the blood gas concentrations have been correlated with changes in the heart as shown by electrocardiographic records.

(2) In dogs premedicated with morphine, bradycardia and arrhythmia are usually present in the different levels of surgical anesthesia produced with cyclopropane. Intravenous injection of amytal abolishes the bradycardia and arrhythmia.

(3) Cardiac irregularities which develop at the time of or soon after respiratory arrest produced by cyclopropane alone may be prevented by barbital or amytal.

(4) These experiments indicate that a barbiturate should be given a clinical trial in place of morphine as preanesthetic medication in patients to be anesthetized with cyclopropane.

REFERENCES

- ¹ Lucas, G. H. W., and Henderson, V. E. A New Anesthetic Gas. Cyclopropane. *Canad. Med. Assn. Jour.*, 21, 173, 1929.
- ² Kurtz, C. M., Bennett, J. H., and Shapiro, H. H. Electrocardiographic Studies during Surgical Anesthesia. *J. A. M. A.*, 106, 434, 1936.

- ³ Seevers, F H, Meek, W J, Rovenstine, E A, and Stiles, J A A Study of Cyclopropane Anesthesia with Especial Reference to Gas Concentration, Respiratory and Electrocardiographic Changes Jour Pharmacol and Exper Ther, **51**, 1, 1934
- ⁴ Robbins, B H, and Baxter, J H, Jr The Relation of Electrocardiographic Changes to the Arterial Concentration of Oxygen, Carbon Dioxide and Cyclopropane in Dogs Anesthetized with Cyclopropane Jour Pharmacol and Exper Ther, **61**, 162, 1937
- ⁵ Meek, W J, Hathaway, H R and Orth, O S The Effects of Ether, Cyclopropane and Chloroform on Cardiac Automaticity Jour Pharmacol and Exper Ther, **61**, 162, 1937
- ⁶ Lieb, C C, and Mulinos, H G Further Observations on Sodium Isoamylethyl Barbiturate as a Laboratory Anesthetic Proc Soc Exper Biol and Med, **26**, 709, 1929
- Shafer, G D, Underwood, F J, and Gaynor, E P The Action of Amytal in Impairing Vagus Cardiac Inhibitory Effects Am Jour Physiol, **91**, 461, 1930
- Gruber, C M, Gruber, C M, Jr, and Colosi, N A The Irritability of the Cardiac Vagus Nerves as Influenced by the Intravenous Injections of Barbiturates, Thiobaituitate and Picrotoxin Jour Pharmacol and Exper Ther, **63**, 215, 1938
- ⁷ Seevers, M H, and Meek, W J Barbiturate Protection from Cardiac Irregularities Induced by Ephedrine Jour Pharmacol and Exper Ther, **48**, 286, 1933, **51**, 287, 1934
- ⁸ Hoff, H E, and Nahum, L J An Analysis of the Cardiac Irregularities Produced by Calcium, and Their Prevention by Sodium Amytal Jour Pharmacol and Exper Ther, **60**, 425, 1937
- ⁹ Jackson, H C, and Ewing, E M Immediate and Subsequent Effects of Anesthesia upon Reflex Cardio-Inhibition Am Jour Physiol, **33**, 30, 1914
- ¹⁰ McCrea, F D, and Meek, W J The Action of Morphine in Slowing the Pulse Jour Pharmacol and Exper Ther, **28**, 361, 1926
- ¹¹ Robbins, B H, Fitzhugh, O G, and Baxter, J H, Jr The Action of Morphine in Slowing the Pulse Jour Pharmacol and Exper Ther, in press
- ¹² Robbins, B H, Fitzhugh, O G, and Baxter, J H, Jr An Analysis of the Factors Controlling the Heart Rate and Rhythm in Dogs Anesthetized with Cyclopropane or with Ether after Premedication with Morphine Jour Pharmacol and Exper Ther, in press
- ¹³ Robbins, B H The Quantitative Determination of Cyclopropane in Air, Water and Blood by Means of Iodine Pentoxide Jour Pharmacol and Exper Ther, **58**, 243, 1936

THE APPLICATION OF CARBAMIDE (UREA) THERAPY IN WOUND HEALING^{*}

HALL G. HOLDER, M.D., AND EATON M. MACKEY, M.D.

LA JOLLA, SAN DIEGO, CALIF.

FROM THE SCRIPPS MEMORIAL HOSPITAL AND THE SCRIPPS METABOLIC CLINIC, LA JOLLA, CALIF.

RECENTLY, Reid¹ pointed out that "it is erroneous to give the idea that the problem of wound healing is essentially synonymous with the principles of asepsis and antisepsis." He notes further, that "among the first of the great principles of wound healing to become established, was the importance of eliminating or preventing the formation of necrosis and debris in wounds." By the removal of dead tissues, bacterial growth is eliminated or reduced to a minimum. Christopher² likewise condemns the use of antiseptics in fresh open wounds, and lists the removal of foreign bodies and devitalized tissues as two of the most important underlying principles in the treatment of fresh wounds. It was the consideration of the importance of this factor which first led us to examine the usefulness of a strong carbamide^{*} (urea) solution, which is a potent agent for dissolving protein substances, such as dead tissues, as a therapeutic agent in wound healing.⁴ This rediscovery of an agent, first used more than three decades ago,⁵ but since forgotten, has produced such good results that an unexpected interest as well as innumerable questions concerning the details of its application to wounds of various types have arisen. It has, therefore, seemed desirable to describe the application of carbamide (urea) in greater detail and to summarize two more years' experience with the product.

The virtues of carbamide have recently been well summarized by Mertins,⁶ essentially as follows:

(1) Carbamide in aqueous saturated solution, by its power of dissolving necrotic debris, removes the chief deterrent to healing in many types of chronic infection.

(2) It is almost totally nonirritating to living tissue.

(3) It is mildly bactericidal to many forms of organisms, especially those producing putrefaction.

(4) It almost immediately eradicates all odor without producing another odor.

(5) It is inexpensive.[†]

* We have adopted the suggestion of a recent reviewer,³ in electing to use the chemical term carbamide, because of the suggested association in the minds of some of the term urea with urine, and also because this substance is now prepared synthetically.

† We are indebted to Rare Chemicals, Inc., of Nepara Park, N. Y., for trial supplies of "eucupin" dihydrochloride.

Submitted for publication June 2, 1938.

These good qualities, which are approximately the same as those which were pointed out in our initial report,⁴ have been supported by all of the observations which we have made since that time. However, two problems have arisen in connection with the use of carbamide. One of these has to do with the physical nature of the material applied to the wound. When we first used carbamide it was applied either in a strong, usually saturated, aqueous solution or in the crystalline form depending on the degree of moistness of a wound. The solution was naturally the method of application of choice in any fistulous wound. Meitins has used it in the aural canal for the treatment of chronic otitis media. In many other areas, the solution could be employed, but we have generally preferred the crystals, when their application was possible. Their chief disadvantage is their tendency to dry out and cake on occasion, and the difficulty of maintaining them in proper contact with the tissue at times. To obviate these difficulties we have compounded a urea paste for occasional use, the preparation of which is described below.

The other problem which we recognized in our early work and which has become important enough to warrant an attempt to obviate it, is the pain which is incident to the use of carbamide in some cases. This is due to the fact that hypertonic solutions may be painful to denuded tissues. Of such origin, is the aggravated pain of an aching tooth when candy is dissolved in the mouth. After a trial of many local anesthetics, a product has been found which is not only effective in almost all cases, on mucosa as well as denuded areas, but also has a useful bactericidal action.⁷ This is iso-amyl-hydrocupicine, which is known as "eucupin". Although originally synthesized as a bactericidal substance, its high potency as a local anesthetic has made it even more useful.^{8, 9} The prolonged anesthesia which results has been particularly useful for our purpose. Since the free base is not water soluble, "eucupin" dihydrochloride is the compound ordinarily utilized. We have mixed this compound with the crystals of carbamide or added it to the solution in a concentration of 0.4-0.5 per cent. It may also be incorporated in the carbamide paste, which is composed of Carbamide 50.0 per cent, karaya gum 2.5 per cent, eucupine 0.5 per cent, and is compounded as follows:

Five hundred Gm. of carbamide* (crystal urea, DuPont) are dissolved in approximately 300 cc. of hot water. Half of this solution is then placed in another container and 25 Gm. of powdered first grade gum karaya (India gum) are dissolved in it by vigorous stirring. The resulting paste is then sterilized by autoclaving. To the other portion of carbamide solution 5 Gm. of "eucupin" dihydrochloride are added and this mixed with the autoclaved carbamide-gum karaya solution, and made up to a final volume of 1,000 cc. This solution on cooling is ready for use.

It has been our practice to treat all infected and, occasionally, some rel-

* Carbamide may be purchased from most chemical houses. A very pure product, which may be obtained at low cost, in quantities of 100 pounds, is crystal urea, manufactured by E. I. DuPont de Nemours & Company, of Wilmington, Del.

atively fresh wounds containing dead tissue, until clean, with carbamide crystals, strong carbamide solutions or the paste. Whether or not the "eucupin" dihydrochloride is added depends upon the pain it causes in the wound, and the type of patient. When the wound is clean and granulating, epithelialization is often completed with other dressings. A word should be said concerning the type of granulation tissue which is obtained by employing carbamide therapy. It is far superior to that which results from the application of many antiseptics or occurs in the presence of infection. The carbamide granulation tissue is healthier and more highly vascularized. It is pink, flat, and ideal for skin grafting. The following cases are presented to demonstrate the principles of carbamide application.

ILLUSTRATIVE CASE REPORTS

Case 1—No 66256 J W, male, age 37, entered Scripps Memorial Hospital December 30, 1936, with typical signs and symptoms of a lobar pneumonia of the right lower lobe. For the first twelve days, although acutely ill, the patient seemed to hold his own. On the twelfth day, his condition was definitely worse with rising temperature, and with clinical and roentgenologic evidence of pyopneumothorax. Aspiration at this time recovered 400 cc of grayish, foul smelling pus, suggestive of lung abscess or anaerobic infection such as is occasionally found following the rupture of a superficial lung abscess into the pleural cavity. Because of the danger of a serious cellulitis of the chest wall with repeated aspiration, immediate open thoracotomy was performed. Under local anesthesia, the eighth rib was resected in the posterior axillary line for a distance of three inches. A large caliber, two-way rubber tube was fastened into the wound for irrigation and drainage. Following the evacuation of a large amount of foul pus, the cavity was irrigated with saturated carbamide solution which was repeated every four hours. There was no evidence of pleurobronchial fistula, but had there been, the use of urea would not have presented such a complication as does Dakin's solution in these cases, as it is not so irritating to the bronchial mucosa. The purulent drainage was deodorized within a few hours—a very helpful property of urea in all foul smelling infections. The clinical course from the time of the thoracotomy showed progressive improvement, the temperature gradually subsiding in two weeks' time, and the patient discharged home, ambulatory, in 21 days, the wound draining very little.

We feel that saturated carbamide solution is far superior to Dakin's solution as an irrigating fluid in empyemata. Its greater lytic properties are more efficient particularly in the anaerobic type of infections, such as detailed above, where control of the infection is directly dependent upon elimination of necrotic tissue on which the bacteria are dependent for their existence. Saturated carbamide solution may best be employed in intracavity infections such as empyemata, nasal sinuses and chronic otitis media, fistulous tracts, as in chronic osteomyelitis, postoperative rectal fistulectomy, ischiorectal abscess cavities, and in deeply infected wounds where the crystals cannot be effectively applied as in deep traumatic wounds and postoperative infected wounds such as the perineal wound following resection of the rectum.

The following case demonstrates the lytic action of carbamide in crystal-line form. At no time did the patient complain of discomfort.

Case 2—No 9400 F W, female, age 23, was admitted to the Scripps Memorial Hospital January 3, 1938, with a history of increasing pain and tenderness over the

sacral region for the preceding four days. Examination showed a healthy adult female whose clinical and laboratory findings were both normal other than the localized painful area. Inspection here revealed a large, tender, indurated, erythematous area. The infection seemed deep and there was no localization suggestive of a furuncle or carbuncle. An exploratory operation, January 5, 1938, demonstrated a large, thickened, infected pilonidal cyst, which was removed by careful dissection down to the posterior sacral attachments. The wound was packed with carbamide crystals and no attempt at closure made. Any remaining necrotic or inflammatory tissue was promptly removed by the carbamide, and the wound rapidly granulated up from the bottom and healed without complications. The tendency for recurrence due to leaving behind a portion of the cyst wall is well known. The use of carbamide with its strong, lytic action on devitalized tissue, is a great aid in cleaning up such a wound and keeping it clean for normal reparative processes and thus reducing the chance of recurrence.

Case 3 demonstrates the use of the carbamide "eucupin" water-soluble paste, necessitated by the pain resulting from application of the crystals.

Case 3—M. G., female, received a third degree burn, November 16, 1937, involving the entire lateral surface of the left thigh from the knee joint to above the iliac crest extending anteriorly to the middle of Poupart's ligament and thence down the anterior surface of the thigh in this same line. The posterior surface of the thigh was involved for about an inch past the junction of the posterior with the lateral surface. This wide area had been treated with tannic acid in the usual manner, but subsequent infection of the burned surface had undermined the crust which had separated in some areas and from such denuded surfaces large amounts of purulent exudate were discharged. The patient had a septic fever with associated constitutional symptoms. On December 4, 1937, dry carbamide crystals were generously applied, and in less than a week's time the majority of the crust and underlying necrotic tissue had been removed. The carbamide crystals then became so painful that the carbamide paste with "eucupin" dihydrochloride was applied. This was well tolerated and very efficacious. Continued use of this paste for two weeks produced a very clean, healthy, granulating surface, ideal for skin grafting. Since the patient was unable to enter the hospital at this time treatment of the burned area was continued with an epithelializing agent and subsequent skin grafting was successful.

The following two cases are presented to illustrate the use of carbamide crystals in traumatic wounds and to demonstrate that the compound may often be applied without discomfort as well as to remove the fear that carbamide may have a deleterious effect on tendons. The blood supply of tendons is notably less than in many other tissues, but in our experience with a number of cases in which tendons were directly exposed to the action of carbamide, even in the presence of suturing and traumatization, we have seen no evidence of a harmful effect.

Case 4—No. 9224. R. G., male, age 4, entered the hospital October 29, 1937, with the history that while playing in the street he was struck and run over by a heavy truck, sustaining a severe injury to the left foot. Physical examination revealed moderate shock as evidenced by pallor, rapid pulse and respirations. There was no evidence of injury other than to the left ankle except subcutaneous emphysema involving the left chest wall and the left side of the neck. Roentgenologic examination showed no evidence of fractured ribs and the laboratory findings were normal. The patient's condition improved after antishock measures were applied and the injured ankle was inspected under ethylene anesthesia. Over the anterior aspect of the left ankle joint the skin was absent as a result of a grinding force which had completely denuded an area two inches in

diameter. It appeared as if the foot had been placed on an emery wheel and a complete section of the soft tissues ground out, including skin, subcutaneous tissue, fascia cruris, sections of the tendons, extensor digitorum longus, hallucis longus and tibialis anticus together with the dorsalis pedis artery and accompanying nerve, ligaments attached to the anterior surface of the talus and the entire articular surface of the talus. The roentgenogram showed the superior margin of the talus ground off so that the articular surface presented a straight line. Operation consisted of debridement of all obviously devitalized tissue. Skin edges were freed and dissected back with the aid of extending incisions above and below. Blood vessels were ligated and repair of the three extensor tendons carried out with lengthening due to loss of substance. The skin defect could not be entirely closed because of the marked tissue loss, but was approximated as well as possible and the foot immobilized at a right angle in a molded plaster splint. At the first dressing, three days later, there was considerable purulent discharge from the wound, and carbamide crystals were introduced generously. The foot was kept immobilized, with only the application of carbamide crystals at the time of the daily dressings. In six weeks the plaster splint was removed, and over the following two weeks gradual weight bearing was allowed with the aid of crutches. The wound was still draining slightly from a small central sinus but in eight weeks' time was entirely healed and the extensor tendons were functioning normally. A mild, acquired talipes valgus was corrected with a leather anklet and arch support, which gave a normally functioning foot.

In this case, as in many others, carbamide was employed without discomfort. In a child with a seriously contaminated, traumatic wound involving soft tissue, tendons, blood vessels, bone and joint surfaces with following infections, deterrents to wound healing were so satisfactorily controlled by the application of carbamide crystals that no injury to the tendon repair occurred, and no serious osteomyelitis developed, leaving an ankle joint without dysfunction. The following case is also a typical example of the good results obtained with carbamide in traumatic injury, involving in addition the presence of gross infection.

Case 5—J. J. L., male, age 45, was first seen at the office October 18, 1937, stating that he had crushed his hand with an air jack hammer while straightening a piece of steel. Examination revealed a three inch laceration on the palmar surface of the right index finger extending from the tip of the distal phalanx to the second palmar crease. The wound was jagged and the adjoining tissues were badly crushed. In addition to the soft tissue injury, there was fragmentation of the bones of the index and second fingers as well as a dislocation of the second phalanx of the first finger. The flexor tendons were exposed throughout the length of the laceration. The wound was debrided under regional anesthesia, the edges sutured as well as possible, and the hand placed on a molded plaster splint. By the third postoperative day, a gross infection developed in the flexor tendon sheath, the wound was opened and packed with carbamide crystals. This was done daily for four days, at the end of which time the wound was clean and granulating. In 10 days' time the wound was completely healed, although traction was maintained on the finger for three weeks, and this was followed by appropriate physiotherapy. Considering the serious tendon sheath infection, the result was excellent, for the only residual disability was a slight limitation of the motion of the second phalanx.

We are still of the opinion that, although the mild bactericidal action of carbamide is of some consequence, the chief value of the compound in wound healing is due to its remarkable solvent action on protein compounds. As Meitins⁶ concludes from his experience with carbamide in chronic otitis media

"the results are simply due to a more adequate removal of the gross and microscopic debris in the recesses of the middle ear, giving nature a fair chance, often with surprisingly successful results" Dilute urea solutions also continue to be used^{10, 11} with the idea that they stimulate cell proliferation in wound healing¹² That they give a slight degree of success we cannot deny, and as we have already pointed out this is probably due to the long known activity of dilute urea solutions in promoting proteolysis of the necrotic tissue¹³ Support is given to this view by a recent study¹⁴ demonstrating that dilute urea solutions are without influence upon the rate of growth of fibroblasts in tissue culture It is true that there is some evidence¹⁵ that dilute urea solutions produce proliferation of capillaries by sprouting and may thus aid in wound healing However, we prefer to avoid dilute urea solutions because of the excellent medium for bacterial growth which they provide and the superior results obtained with higher concentrations

SUMMARY

The efficacy of carbamide (urea) as an adjunct to wound healing, due primarily to the lytic action of strong aqueous solutions upon necrotic tissue and other debris, is again demonstrated Details of the practical application of carbamide therapy are outlined

REFERENCES

- ¹ Reid, Mont R ANNALS OF SURGERY, 105, 982, 1937
- ² Christopher, Frederick Internat Clin, Vol 1, n s, 81, March, 1938
- ³ Fantus, Bernard The 1937 Year Book of General Therapeutics, The Year Book Publishers, Inc, Chicago, p 261
- ⁴ Holder, Hall G, and MacKay, Eaton, M J A M A, 108, 1167, 1937
- ⁵ Symmers, W St C, and Kirk, T S Lancet, 2, 1237, 1915
- ⁶ Mertins, Paul S, Jr Arch Otolaryngol, 26, 509, 1937
- ⁷ Morgenroth, J, and Ginsberg, S Berl klin Wchnschr, 1, 343, 1913
- ⁸ Dixon, W E, and De P Jour Pharm and Exper Therap, 31, 407, 1937
- ⁹ Kilbourne, Normal J Jour Surg, Gynec, and Obstet, 62, 590, 1936
- ¹⁰ Lewy, Robert B Arch Otolaryngol, 25, 178, 1937
- ¹¹ Bogart, Leon M J Mich Med Soc, 36, 285, 1937
- ¹² Robinson, William Am Jour Surg, 33, 192, 1936
- ¹³ Ramsden, W J Physiol, 28, 23, 1902
- ¹⁴ Hetherington, Duncan C, and Shipp, Mary E Proc Soc Exper Biol and Med, 37, 238, 1937
- ¹⁵ Abel, Richard Anat Rec, Supplement No 3, 67, 1, 1937

GAS GANGRENE[†]

E DUNBAR NEWELL, M D

CHATTANOOGA, TENN

After my experience in the Evacuation Hospitals of the A E F I thought I was thoroughly competent to diagnose and treat patients with gas gangrene, but, just one year ago, I lost a patient from this condition, and then I realized that I knew very little about the present-day diagnosis and treatment of gas bacillus infection. I, at once, began to review the literature extensively. My opinion is that probably all the papers on this subject written before 1934 are worthless for clinical purposes. However, an article, by Eliason,¹ in 1937, is most comprehensive and instructive.

Gas bacillus infections occur in all sections of the United States. In some localities it is far more prevalent than in others. In my section—Chattanooga—it is very rare. The Baroness Erlanger Hospital, a 200 bed municipal hospital in Chattanooga, reports no cases during the period 1926–1934, and only two cases each in 1935–36–37–38. Of the eight cases reported by Erlanger Hospital, three were gunshot wounds, three were compound fractures, one a crushed arm, and one an abscess over the orbit. In over 42,000 traumatic cases treated at our clinic during the past 21 years, our records show only five cases of gas bacillus infection—one severe trauma to the leg, one compound fracture, two gunshot wounds, and one avulsion of the arm. In 257 major compound fractures during the past 12 years, there has been only one case of gas gangrene.

Millar² records a series of 607 cases occurring in civil life, which is probably only a small percentage of the cases of gas bacillus infection that did develop during that period—the others were not reported.

Junghous, in 1933, analyzed more than 60 cases of gas gangrene following hypodermic medication of all types, of which only four survived. Boland, of Atlanta, says "In 80 cases of compound fractures, occurring in Negroes, 15, or 19 per cent, developed gas gangrene, whereas, in the same period, in 97 cases of compound fractures, occurring in white, 7 per cent developed gas gangrene."

Eliason¹ says that at the University of Pennsylvania and Philadelphia General Hospitals, the incident of gas gangrene following amputation for diabetic gangrene, senile gangrene, and Buerger's disease was 6.8 and 10 per cent, respectively.

In our clinic, over 100 amputations for arteriosclerotic and diabetic gangrene have been performed and no case of gas gangrene has been recorded. Evidently this porous, sandy, hilly soil does not harbor anaerobic organisms to the same extent that a flat country does. Cultures and smears from the

[†] Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 6, 7, 8, 1938.

wounds and skin of the patients who come to our clinic are rarely positive for the anaerobic organisms. Cultures from the battlefields of France, as well as from the uniforms on men returning from the trenches, were 100 per cent positive for anaerobic organisms, according to records from the Surgeon General's office.

In civil life, chronic leg ulcers have shown 34.3 per cent positive. Roberts, Johnson,³ and Buckner⁴ were able to cultivate it from the skin of 21.7 per cent of unprepared abdomens, 8.5 per cent of knife blades used in making skin incisions, and 9.2 per cent from the peritoneum when opened for noninflammatory conditions. Gamble reported 12 cases of emphysematous gangrene of the abdominal wall which he has had in his practice since November, 1923—all of these cases followed operation for ruptured, gangrenous appendicitis.

There have been about 25 varieties of anaerobic organisms isolated. *Clostridium welchii* is present in from 80 to 90 per cent, *Clostridium oedematis maligni* or vibrio septique of the French, 10 to 20 per cent, *Clostridium oedematiens* about 5 per cent.

The usual prophylactic polyvalent dose is 1,500 units of tetanus antitoxin, 2,000 units of *Clostridium welchii* antitoxin, and 2,000 units of *Clostridium oedematis maligni*. The usual therapeutic dose, called polyvalent gas gangrene antitoxin, comprises the following in one vial: 10,000 units *Clostridium welchii*, 10,000 units *Clostridium oedematis maligni*, 2,500 units *Clostridium histolyticum*, 1,000 units *Clostridium oedematiens*, and 200 units oedematoids. This combination contains antitoxin specific for all the toxin-producing, spore-forming anaerobes now credited with causing gas gangrene in man.

Diagnosis—It has been thought for years that crepitation in the tissue was the first symptom that caused one to suspect gas gangrene. It is now known that we must make the diagnosis of gas bacillus infection before crepitation is perceptible, or we lose the precious early hours of the infection when proper management will give a mortality of from 5 to 15 per cent instead of the usual mortality of from 49 to 80 per cent.

It is so usual to read the statement that the positive diagnosis of the contaminating agent is made by smears and cultures¹. The positive findings by smear may mean nothing, as Evacuation Hospital No. 8 of the A. E. F. reported 890 wound cultures of which 478, or 53 per cent, contained anaerobic bacilli, of these 478 wounds, 67 per cent at no time showed evidence of gas gangrene. To await the result of culture before making a diagnosis is too late. The diagnosis must be suspected when a patient who has a wound that has been contaminated with soil, feces, or dirty clothing suddenly complains of severe pain in the wound, when the pulse rate is higher than the temperature would indicate, and inspection of a previously closed wound reveals edema and brownish discoloration of the skin. If not closed, the wound is dirty in appearance and there is a discharge of brownish serum, and, at times, a mousy, offensive, or putrid odor, or there may be scarcely no odor. If, in addition to the above signs and symptoms, a roentgenogram shows gas bubbles in the tissue, active treatment should be begun at once.

Rinehart was first to call our attention to the value of the roentgenogram in making a diagnosis before the infection is clinically apparent. In suspected cases a roentgenogram should be made every four hours. If there is an increase in the number of air bubbles in each succeeding film, then we know that the bubbles are not due to air that has been forced into the tissue by muscle action at the time of the injury. Too, the gas in the tissue may be due to colon bacillus infection. The roentgenologic diagnosis is usually many hours ahead of the clinical diagnosis, and an early diagnosis is of supreme importance.

If the infection is due to vibration septique, no crepitation will be found on palpation and no gas bubbles will be found roentgenologically. The diagnosis will be made by the very marked edema. Ghormley⁷ reports such a case in his series of 43 cases from The Mayo Clinic.

Frequent inspection of the patient and the wound is of extreme importance during the early stages. Early recognition is the most important step in treatment and is not difficult if the possibility of gas gangrene is kept constantly in mind.

Treatment—The most important factor in the treatment is the recognition that where muscle tissue is mangled and the blood supply is gravely damaged, one has the ideal culture medium for the growth of anaerobic organisms and that without this condition the presence of these organisms should give us but little concern.

Since our war service, it has been our practice to clean wounds with soap and water, to undertake a meticulous debridement whenever soft parts have been mangled, to control bleeding by direct attack, and not to stop bleeding by packing the wound, thus further impairing the blood supply. If debridement and hemostasis are satisfactory and the wound can be closed without tension, then the wound is closed without drainage. At the State Hospital in Shreveport, Louisiana, the incidence of gas bacillus infection has been greatly reduced by not closing such wounds.

During the past 10 years, we have used combined prophylactic tetanus and gas gangrene antitoxin whenever the wound has been greatly traumatized and grossly contaminated with soil, *etc.* In four of the five cases occurring in our clinic, the prophylactic antitoxin was administered, the first, or other case, occurred before we had begun the routine use of the prophylactic antitoxin. However, during the 20 years previous to the past 10 years, no prophylactic dose was administered and only one case is recorded during that 20-year period. Erlanger Hospital, of Chattanooga, did not use prophylactic injections during the same period and although with a greater number of traumatic cases treated, had no case of gas gangrene for nine years. It is generally concluded that the prophylactic injection does not prevent gas bacillus infection, but that it probably lengthens the incubation period and lessens the severity of the attack, and that it should be given on three successive days.

Veal,⁶ of New Orleans, says "There were two deaths among the 27 patients who had received the prophylactic antitoxin, a mortality of 7.4 per

cent, while there were 13 deaths among the 27 who did not receive it, a mortality of 48 per cent. Furthermore, in the group of 10 patients treated by débridement, all of whom received prophylactic antitoxin, there was only one death and this patient was almost moribund when he was first seen."

It is widely practiced and generally believed that early thorough débridement is the surest preventive against gas gangrene and one of the most important measures to stop the spread of the infection after it has begun. The débridement must consist of an amputation if the blood supply has been greatly damaged, and this must be performed early and should be, of course, of the guillotine type. If the blood supply is fair to good, then under the modern treatment an amputation will probably not be necessary.

From our own experience and from the literature, the one most important therapeutic agent is the early intravenous administration of 10,000 to 30,000 units of polyvalent antitoxin, repeated every six to eight hours. Bohlman,⁸ of Johns Hopkins, has suggested the use of sulfanilamide for both prophylaxis and therapeutics.

The Surgeon General's report calls attention to symbiosis of various aerobes and anaerobes. In Base Hospital No. 15, AEF, in 73 cases of gas gangrene with death, activity of gas bacilli was self-limiting and probably confined to the first week after the wound was received, with a drop in anaerobes from 38 to 7 per cent during the first seven days, as the common pyogens *Streptococcus* and *Staphylococcus* accumulated rapidly in the wound. The symbiotic effect was particularly prominent in fatal wounds. For its effects on both aerobes and anaerobes, it should be given in all cases.

Kelly⁷ reports 44 cases of gas gangrene of the extremities, treated with 100 mg. of penicillin. There were 29 in which amputation was not performed and all 29 patients recovered. Out of the 15 who had amputation, five died, a mortality of 33.3 per cent. He says further: "In concluding, it seems fair to state that the 100 mg. day, up to this time, seems to be definitely established as an aid in the treatment of gas gangrene, both in extremity and in trunk cases, but it seems desirable to use serum and other measures and refrain from amputation until the patient has recovered from shock and from the gas bacillus infection."

For local application or instillation, we formerly always used Dakin's solution by the meticulous method elaborated by Dr. Alexis Cannel, at the Rockefeller Institute, but, judging from the present-day literature, it seems to make little difference whether Dakin's solution, hydrogen peroxide, or 1-500 potassium permanganate is used.

Case Report—On February 6, 1938, I saw a patient in consultation at Dayton, Tenn. Twenty-four hours previously this young man had been shot in the abdomen, on the right side just below the costal arch, with a shotgun. An exploratory celiotomy had been performed almost immediately by Dr. Agnew Thomson, appendectomy had been performed as the appendix was in the wound. The lower edge of the liver was found lacerated and the anterior surface of the liver was speckled with shot. Multiple shot were in the mesentery and serous coat of intestines, however, no perforation of the intestine was found. The lower intercostal and abdominal muscles of the right side

were torn and lacerated. The wound was closed and a small rubber tissue drain placed under the skin. When first seen, the temperature was 102° F, pulse 124, and the wound was edematous and soggy in appearance and was reddish brown in color, a brownish, offensive serum was exuding between the sutures and from the drain, on palpation, crepitation could be felt for an area of six inches below the wound. When the sutures were removed gas could be seen bubbling up from the wound surfaces and from the area under the intact skin. Remembering Kelly's experience with amputation, I did not advise further incisions to drain the crepitating area. The wound was kept moist with H₂O₂ packs and 20,000 units of polyvalent gas gangrene antitoxin were given intravenously immediately, and 120,000 units more were administered over a period of three days.

Sulfanilamide was given in 10 grain doses every four hours for six days. Temperature was normal on February 13, and the sulfanilamide was discontinued. No evidence was present at this time of gas bacillus infection. However, on February 20, two weeks after onset, the temperature rose again, sulfanilamide was reinstituted at four-hour intervals for three days, when the temperature again became normal. Roentgenotherapy was administered twice daily during the first week.

Although this patient was desperately ill with high temperature and was delirious, at the end of the first week he was practically over the gas bacillus infection. The sulfanilamide must have prevented the symbiosis which is so common in these cases.

REFERENCES

- ¹ Eliason, E. L., Erb, W. H., and Gilbert, P. D. The Clostridium Welchii and Associated Organisms, a Review and Report of 43 New Cases. *Surg., Gynec., and Obstet.*, 64, 1005, June, 1937.
- ² Millar, W. M. Gas Gangrene. *Surg., Gynec., and Obstet.*, 54, 232, 1932.
- ³ Johnson, W. W. Gas Gangrene Infections Following Appendectomy. *Am. Jour. Surg.*, 33, 141-147, July, 1936.
- ⁴ Brickner, W. M., and Milch, H. Surgical Clinics from the Broad Street Hospital. Gas Gangrene Infections. *Internat. Clin.*, 4, 1926.
- ⁵ Ghormley, R. K. Gas Gangrene and Gas Infections. *Jour. Bone and Joint Surg.*, 17, 907, October, 1935.
- ⁶ Veal, J. R. A Study of Gas Bacillus Infection, with Special Reference to Its Occurrence in the Negro. *New Orleans Med. and Surg. Jour.*, 98, 432, February, 1937.
- ⁷ Kelly, J. F., and Dowell, D. A. Present Status of the X-rays as an Aid in Treatment of Gas Gangrene. *J. A. M. A.*, 107, 1114-1117, October 3, 1936.
- ⁸ Bohlman, H. R. Gas Gangrene Treated with Sulfanilamide. *J. A. M. A.*, July 24, 1937.

DISCUSSION.—DR. J. DUFFY HANCOCK, Louisville, Ky. I think Doctor Newell's paper is most timely, as well as most interesting. With the advent of high speed transportation I believe we will see many more of these crushing injuries and probably an increase in gas gangrene infections. He has presented an excellent summary of the modern treatment of gas bacillus infection. I would like to report another case—a woman, age 45, whose right forearm was injured in an automobile accident, fell into the hands of an excellent country doctor who cleansed the wound, left it open and gave a prophylactic dose of the combined anti-gas gangrene and antitetanic serum. Twelve hours later she had intense pain in the forearm, with a foul discharge. Twenty-four hours after the injury, when I saw her, there was crepitation to the elbow, a smear was positive for the gas bacillus of Welch and this was confirmed later by culture. We followed essentially the same treatment as Doctor Newell.

described, opened the wound and used hydrogen peroxide irrigations, administered the serum, and sulfanilamide, 90 gr the first day, 60 the second and 30 the third, and administered iointgenotherapy, 120 r units every day for four days. She went on to a complete recovery.

Just as Doctor Newell said, I believe treatment has been revolutionized in the last few years, and that in the future it will consist of iointgenotherapy, serum, sulfanilamide and irrigations, with hydrogen peroxide being the solution I think is best of all.

DR RALPH G. CAROTHERS, Cincinnati, Ohio. I agree with everything Doctor Newell has said except as to the use of iointgenotherapy. Doctor Newell pointed out that there was a great deal of gas gangrene in some localities, and in others not so much. I think that is so, the infection is much more virulent in certain parts of the country than in others. In talking to a surgeon from Wyoming, he told me recently that he had not seen a case of tetanus in that part of the country. Of course, tetanus is not gas gangrene, but they are caused by similar organisms. I wonder if Doctor Kelly's work is not based on a type of organism that is prevalent in the dry plains of Nebraska, which are similar to the Wyoming locality I referred to. Doctor Cubbins reported eight cases treated with iointgenin in Cook County Hospital, Chicago, with eight deaths.

In Cincinnati, we have a type of organism that is rather virulent. I saw a case of gunshot wound in the thigh with a compound fracture of the femur. The accident occurred at three o'clock in the afternoon and when the patient was brought in at 6:30, the iointgenogram showed the infection to be already well advanced.

The principal thing in addition to the serum is to decompress the parts and split the fascia on both sides. The gas is like an expanding tourniquet. If you split the fascia on the two sides, expansion can take place without cutting off the blood supply. We did this in this case, and then put the patient in a Thomas splint. The swelling was so great that the thigh bulged over the splint on each side, but the tissues did not become gangrenous and there was no edema below the knee. That man has a good leg today.

DR GROVER C. WEIL, Pittsburgh, Pa. The paper presented by Doctor Newell considers a very important factor in traumatic surgery, and certain phases of it have been very interesting from the point of view of treatment. Our experience in gas bacillus infection dates back many years, in view of the large number of traumatic cases we have had on the service of the Pittsburgh Coal Company.

The advances made in the treatment of such infections, as I review them, seem almost like a romance in surgery, dating back to the days when immediate amputation was found necessary in order to save the life of the patient, and up to the present date with the use of antitoxin as one of the important therapeutic measures. The heavier mortality in the older days seems to have been due to lack of proper understanding in diagnosis.

A great factor in the saving of lives at the present time on our service is the early recognition of the condition and the immediate institution of surgical measures. One important diagnostic feature, as we instruct our medical students, is the value of detecting a "sour-sweet" smell which emanates from the wound and which can be detected early when one becomes familiar with the odor. On many occasions the nurses have reported its presence, which always serves as an indication for an immediate examination of the wound, and one can then observe the physical changes indicating the infection. I feel that many lives have been saved as the result of the early detection of this

diagnostic sign. Surgical measures are immediately instituted in the way of large incisions and proper drainage, followed by the application of huge wet compresses far beyond the site of the lesion, using as a rule magnesium sulphate. We immediately administer huge doses of antitoxin, which has proved of utmost value on our service.

With reference to the advantages of roentgenotherapy, I may say that our experience has been rather limited and I would rather hesitate to rely solely upon its administration as a therapeutic measure, in view of its terrific violence and the powerful invasive properties of certain of these organisms. As a preliminary measure, however, until the patient can be transported to a suitable institution where proper therapy can be instituted, one may be justified in its application.

DR E DUNBAR NEWELL, Chattanooga, Tenn. (closing). I reported one case where I did not use an incision to relieve the tension. That has always been my practice. In war surgery we had to do that, but in this particular case I thought if Kelly had the same kind of organism that we had and reported such wonderful results, I would give it a trial. I did so, and while one case does not mean anything it seemed to be very effective. These are desperate cases, and patients are in profound shock when they get this infection, and maybe we do harm by further manipulation.

My purpose was to bring out that this treatment which is so effective in the hands of a few men might be used by many more. After all, none of our old methods was very effective. I agree with Doctor Carothers as to the violence of the organisms. In our particular section we do not see so much of it, and in other sections it is very common.

Before reading the recent literature, I thought I was well qualified to both diagnose and treat gas bacillus infections, but after I had concluded my reading I was amazed to find out how little I knew about the modern methods of drugs and treatment.

FRACTURES AND DISLOCATIONS BY MUSCULAR VIOLENCE, COMPLICATING CONVULSIONS INDUCED BY METRAZOL FOR SCHIZOPHRENIA*

LOUIS CARP, M D

NEW YORK, N Y

FROM THE NEW YORK STATE DEPARTMENT OF MENTAL HYGIENE, DR WILLIAM J TIFFANY, COMMISSIONER

THE MONTHLY REPORT to the Board of Visitors of the Rockland State Hospital for May, 1938, mentioned a fractured neck of a femur in a female schizophrenic, age 30, which had been produced by the muscular violence of a convulsion induced by metrazol. This injury seemed so severe and unusual that statistics on similar injuries were obtained from the 20 New York Civil State Hospitals according to a definite scheme of study (Table I). These statistics are analyzed in Table II, and they indicate that the complicating injuries must be seriously considered in appraising the value of metrazol therapy.

It is clearly not within the scope of this paper to give the clinical features or treatment of the injuries. Suffice it to say that 687 patients had metrazol therapy one or more times, and that 12 fractures (1.78 per cent) and 118 dislocations (17.2 per cent) occurred in these patients as complications of the convulsions. In terms of the total number of convulsions (859) in all the patients up to the time of injury, the fractures constituted 1.5 per cent and the dislocations 13.9 per cent.

In no instance was there any external violence, such as an injury sustained by falling out of bed. In every case, the injury was produced entirely by the muscular violence of the convulsion.

By comparison, the convulsive state produced by epilepsy shows that none of the injuries under discussion have occurred at the Rockland State Hospital during the past three years. During this time, the average number of epileptics under observation monthly was 30, and these patients had an average number of 213 convulsions monthly.

A few psychiatrists mention injuries of the same nature. Finkelman, Steinberg and Liebert¹ report "minor complications such as dislocation of the mandible and dislocation of the head of the humerus", Nightingale² reports a "fractured femur", Dhunjibhoy³ reports one dislocated shoulder in 12 cases treated, and Lebensohn⁴ reports "dislocation of the shoulder."

History of Shock and Convulsion Therapy—In 1933, Sakel⁵ described the treatment of morphine addiction by the use of massive doses of insulin with its resulting hypoglycemia. In 1934, he⁶ described the insulin hypoglycemic shock therapy for schizophrenia. The treatment "grew out of the

Submitted for publication February 1, 1939.

* 1,404 patients had insulin therapy. One sustained a dislocation of the mandible, three had dislocations of the head of the humerus, and one had a fracture of the greater tuberosity of the humerus, all the result of muscular violence during a hypoglycemic convulsion. These cases are included in Table I.

TABLE I
STATISTICAL DATA IN 13 FRACTURES AND 120 DISLOCATIONS PRODUCED BY MUSCULAR VIOLENCE OF CONVULSIONS DURING
METRAZOL AND INSULIN THERAPY

Name of State Hospital	Total Number of Patients Treated		Initials of Patients	Sex	History Number	Age	Number of Convulsions Previous to Injury	Duration of Convulsive Seizure Pro- ducing Frac- ture or Dislocation	Type of Restraint	Anatomic Diagnosis
	Metra- zol	Insu- lin								
Binghamton	37	70	S H C	M	228552	33	4	50 secs	None	Fracture anatomic neck hu- merus, fracture greater tuberosity, posterior dis- location head merus
Brooklyn	343	251	T L	F	55843	38	6	46 secs	None	Anterior dislocation head hu- merus
			E J	F	54956	27	6	45 secs	None	Anterior dislocation head hu- merus
			L O	M	46035	33	15	50 secs	None	Intracapsular fracture neck femur
			S L	M	52825	24	16	50 secs	None	Intracapsular fracture neck femur
Buffalo	35	86	H B	M	42530	26	4	70 secs	None	Dislocation mandible
			E C	M	52488	23	15	46 secs	None	Dislocation mandible
			J D	M	52692	22	0	48 secs	None	Dislocation mandible
			B S	M	55347	35	22	54 secs	None	Dislocation mandible
			A O	M	48502	30	0	57 secs	None	Dislocation mandible
			R M	M	53220	19	13	50 secs	None	Dislocation mandible
			F L	M	50440	33	0	52 secs	None	Dislocation mandible
			M J	M	50453	25	0	45 secs	None	Dislocation mandible
			A C	F	51597	28	7	48 secs	None	Dislocation mandible
			K F	F	51898	32	14	54 secs	None	Dislocation mandible
			E K	F	51473	30	1	45 secs	None	Dislocation mandible
			I S	F	55215	25	2	50 secs	None	Dislocation mandible
			A S	F	41391	33	1	47 secs	None	Dislocation mandible
			E S	F	54380	20	1	45 secs	None	Dislocation mandible
			A C	M	54869	24	0	36 secs	None	Dislocation mandible
			A C	M	54869	24	2 (insulin)	63 secs	None	Dislocation mandible
			E M	F	24346	31	21	1 min	None	Dislocation head right hu- merus
			E M	F	24346	31	31	1 min	None	Dislocation head left hu- merus
										Dislocation man- dible 12 times

FRACTURES AND DISLOCATIONS

Central Islip	25	111	C J	M	25561	24	6	1 min	40 secs	None	Dislocation mandible 7 times in 7 convulsions
			J M	M	25697	44	7	1 min	10 secs	None	Dislocation head humerus
			G M	M	23666	27	10	1 min	50 secs	None	Dislocation head humerus
			M D	M	29581	34	0	1 min	20 secs	None	Intracapsular fracture neck femur
Creedmoor	33	53	G A P	M	27969	36	4	1 min		None	Intertrochanteric fracture neck femur
			J B	M	32777	32	33	1 min		None	Fracture greater and lesser tuberosity humerus
			V B	F	23546	20	0	1 min		None	Dislocation mandible
			V B	F	23546	20	13	1 min		None	Dislocation mandible
Gowanda	41	35	N F	M	32070	21	3	1 min		None	Dislocation mandible
			J T	M	291938	30	7		50 secs	None	Fracture anatomic neck humerus
			D B	M	239618	26	2		45 secs	None	Dislocation mandible
			M P	M	304992	28	1		54 secs	None	Dislocation mandible
Harlem Valley	11	126	M P	M	304992	28	2		56 secs	None	Dislocation mandible
			M P	M	304992	28	3		51 secs	None	Dislocation mandible
			F J E	M	291940	30	0		54 secs	None	Dislocation mandible
			W G	M	258792	28	10	2 1/2 mins		None	Dislocation mandible
Hudson River	15	100	E H	M	269314	30				None	Dislocation mandible
			G K	M	238614	30	0			None	Dislocation head humerus
			H H	M	288689	37	1			None	Dislocation head humerus
			R V L	M	284654	23	33	1/2 min		None	Anterior dislocation head humerus
Hudson River	15	100	M G	M	307391	33	21		45 secs	None	Compression fracture body seventh thoracic vertebra, dislocation mandible
			I S	F	306461	38	26	1 min		None	Fracture transverse processes fifth lumbar vertebra
			H F	F	35608	22	1	2 mins		Manual	Dislocation head humerus
			B C	F	33149	40	0	1 min	30 secs	Manual	Dislocation mandible
Hudson River	15	100	B C	F	33149	40	6	1 min		Manual	Dislocation mandible
			B C	F	33149	40	9	1 min		Manual	Dislocation mandible
			B C	F	33149	40	11	1 min		Manual	Dislocation mandible
			B C	F	33149	40	12	1 min		Manual	Dislocation mandible
Hudson River	15	100	B C	F	33149	40	13	1 min		Manual	Dislocation mandible
			B C	F	33149	40	14	1 min		Manual	Dislocation mandible
			B C	F	33149	40	16	1 min		Manual	Dislocation mandible
			B C	F	33149	40	19	1 min		Manual	Dislocation mandible
Hudson River	15	100	B C	F	33149	40	21	1 min		Manual	Dislocation mandible
			B C	F	33149	40	22	1 min		Manual	Dislocation mandible
			B C	F	33149	40	23	1 min		Manual	Dislocation mandible
			B C	F	33149	40	24	1 min		Manual	Dislocation mandible

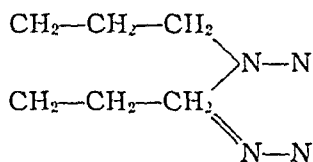
TABLE I—(Continued)

Name of State Hospital	Total Number of Patients Treated		Initials of Patients	Sex	History Number	Age	Number of Convulsions Previous to Injury	Duration of Convulsive Seizure Pro- ducing Frac- ture or Dislocation	Type of Restraint	Anatomic Diagnosis
	Meta- zol	Insu- lin								
Kings Park Manhattan			B C	F	33149	40	26	1 min	Manual	Dislocation mandible
			R T	F	32372	33	0	1 min	Manual	Dislocation mandible
	1	96	F A	M	275165	25	7	52 secs	None	Fracture angle mandible
	13	35	R S	F	93943	28	2	65 secs	None	Dislocation mandible
			J C	M	101026	26	0	95 secs	None	Dislocation mandible
Marcy	17	52	A B	F	308735	33	2	1 min	Partial, free- dom of ex- tremities	Dislocation mandible
			C D	F	307574	28	3	1 min	Partial, free- dom of ex- tremities	Dislocation mandible
Psychiatric In- stitute Rockland	0	82	I H	M	1642	33	1 (insulin)	45 secs	None	Dislocation head humerus
	102	53	J U	M	8690	28	0	1 min	None	Anterior dislocation head humerus, fracture greater tuberosity
			R S	F	867	30	2	1 min	Light protec- tion sheet	Fracture neck femur
			H N	F	11592	31	7	1 min	None	Anterior dislocation head hu- merus
			F G	M	10162	29	0	55 secs	None	Dislocation mandible
			F G	M	10162	29	1	55 secs	None	Dislocation mandible
			F G	M	10162	29	4	55 secs	None	Dislocation mandible
			V B	M	11253	25	10	1 min	None	Anterior dislocation head hu- merus
			L H	M	5434	26	1	55 secs	None	Dislocation mandible
			L H	M	5434	26	2	55 secs	None	Dislocation mandible
			L H	M	5434	26	3	55 secs	None	Dislocation mandible
			L H	M	5434	26	4	55 secs	None	Dislocation mandible
			L H	M	5434	26	5	55 secs	None	Dislocation mandible
			J N	M	9859	23	0	55 secs	None	Dislocation mandible
			J N	M	9859	23	1	55 secs	None	Dislocation mandible
			J N	M	9859	23	9	55 secs	None	Dislocation mandible
			J N	M	9859	23	14	55 secs	None	Dislocation mandible
			J N	M	9859	23	19	55 secs	None	Dislocation mandible
			A S	M	5769	33	0	55 secs	None	Dislocation mandible
			A S	M	5769	33	10	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible
			A S	M	5769	33	20	55 secs	None	Dislocation mandible

	T	B	F	2218	26	0	65 secs	None	Dislocation mandible	
	T	B	F	2218	26	2	65 secs	None	Dislocation mandible	
	T	B	F	2218	26	6	65 secs	None	Dislocation mandible	
	T	B	F	2218	26	8	65 secs	None	Dislocation mandible	
	B	M	F	11781	21	8	50 secs	None	Dislocation mandible	
	M	W	F	10885	23	0	1 min	None	Dislocation mandible	
	M	W	F	10885	23	18	1 min	None	Dislocation mandible	
	P	J	M	11540	18	0	45 secs	None	Dislocation mandible	
	C	M	M	944	17	6	55 secs	None	Dislocation mandible	
	S	M	M	6853	19	3	55 secs	None	Dislocation mandible	
	S	M	M	6853	19	14	55 secs	None	Dislocation mandible	
	J	S	M	12184	30	0	55 secs	None	Dislocation mandible	
	J	S	M	12184	30	5	55 secs	None	Dislocation mandible	
	S	B	F	12146	20	19	40 secs	None	Dislocation mandible	
	M	D	F	11339	23	0	45 secs	None	Dislocation mandible	
	M	D	F	11339	23	1	45 secs	None	Dislocation mandible	
	M	D	F	11339	23	4	45 secs	None	Dislocation mandible	
	M	D	F	11339	23	6	65 secs	None	Dislocation mandible	
	M	D	F	11339	23	15	65 secs	None	Dislocation mandible	
	M	M	F	10797	31	0	10 secs	None	Dislocation mandible	
	M	W	F	10014	29	0	55 secs	None	Dislocation mandible	
	M	W	F	10014	29	2	55 secs	None	Dislocation mandible	
	M	W	F	10014	29	5	55 secs	None	Dislocation mandible	
	M	W	F	10014	29	6	55 secs	None	Dislocation mandible	
	M	W	F	10014	29	13	55 secs	None	Dislocation mandible	
St Lawrence	P	E	W	26439	39	0 (insulin)	15 secs	None	Fracture greater tuberosity humerus, anterior dislocation head	
	F	C	M	30801	21	3	30 secs	None	Dislocation mandible	
Willard	F	C	M	30801	21	4	1 min	None	Dislocation mandible	
	J	S	M	309779	35	0	2 mins	None	Dislocation head humerus	
Middletown	W	T	R	313254	21	4	1 min	None	Dislocation head humerus	
Pilgrim	No injuries									
Rochester	No injuries									
Syracuse	No injuries									
Psychopathic	(no treatment given)									
Utica	No injuries									
	Insulin	Male	Female	Average Age	Largest Number of Convulsions Previous to Injury	Number of Cases Injured During Initial Convulsion	Average Duration of Convulsive Seizures	Percentage with No Restraint	Fractures	Dislocations
Totals	687	1,404	46	29 yrs	33	24	1 min	83 76%	13	120

insulin borderline therapy for morphine addiction" Convulsions occasionally occur, and recently psychiatrists⁷ have considered them an asset in therapy

In 1929, Nyiló and Jablonsky⁸ observed that schizophrenics who also had epilepsy were apparently improved after epileptic seizures. Similar observations were made by Muller,⁹ in 1930, and by Glaus,¹⁰ in 1931. In 1934, von Meduna¹¹ of Budapest, conceived the idea of using convulsant drugs in schizophrenia. "The theoretical basis for the therapy is the assumption that a certain biochemical antagonism exists between the convulsive state and the schizophrenic process." He proved the impracticality of a number of the convulsant drugs and then he used 25 per cent camphor in olive oil intramuscularly. This preparation was unreliable in its effects, insoluble, toxic and painful. In 1935, he¹² employed the preparation known as cardiazol, which is marketed in this country as metrazol. Its intravenous administration produced prompt convulsive seizures without the disadvantages of the convulsant drugs which had been used previously. The drug itself is a white crystalline powder, readily soluble and bears the chemical name of pentamethylenetetrazol which has the following structure



Technic of Administration—Metrazol is prepared in 10 per cent aqueous solution, ready for intravenous use, so that 10 cc represents 1 Gm. The dose is from 3 to 15 cc, the amount employed varying with the receptivity and sensitivity of the patient to violent convulsive seizures. The treatment is administered before breakfast with the patient in bed. The use of restraint depends upon his motor activity. With the proper nurse assistance, the metrazol solution is injected intravenously as rapidly as possible. This is necessary because the drug is excreted very quickly and because a massive therapeutic effect on the cortex is desirable.

Description of a Typical Convulsion—Metrazol therapy was observed by the author in 43 males and 30 females, and was administered by Dr Charles M. Holmes at the Rockland State Hospital. A few seconds after the metrazol is injected, its effect is evidenced. The reaction pattern depends in some measure on the patient's receptivity. Convulsions may be either petit mal or grand mal in type. The latter are desired and they are pertinent to this paper. There is frequently an aura which is described in various ways by patients. Flashes of light, darting of bizarre figures, visualization of a ball of fire, a sense of compression of the chest and difficulty in respiration. Some patients are apprehensive and others frightened and complaining. There is a prompt, pungent odor to the breath which is rapidly dissipated. There may be a short cough, terror of the impending convulsion, quick closure and opening of the eyelids and a yawn. At this point, a soft gag is inserted between the teeth to prevent biting of the tongue. In a few seconds,



FIG 1—Case No 867 Fracture of the neck of the femur in a female, age 30



FIG 2—Case No 11253 Anterior dislocation of the head of humerus in a male, age 25



FIG 3—Case No 8690 Anterior dislocation of head of humerus with fracture of greater tuberosity in a male, age 28



FIG 4—Case No 307391 Compression fracture of the seventh thoracic vertebra in a male age 33

the convulsion begins with slight twitching, and very quickly it becomes clonic, tonic, or a mixture of both. The patient becomes unconscious, the eyes deviate, the pupils dilate and there is an initial pallor followed by extreme suffusion of the face. In some cases, there is a tendency for the upper extremities to be thrown upwards. As a rule, there is complete extension at the elbow and volar flexion at the wrist with bizarre flexion of the fingers and adduction of the thumb. The tonicity of the muscles is so great that the pulse cannot be felt. The lower extremities are completely extended at the knee and there is plantar flexion at the ankle joint and



FIG 5—Case No 275165 Fracture of the angle of the mandible in a male, age 25



FIG 6—Case No 228552 Fracture of the anatomic neck of the humerus and the greater tuberosity with posterior dislocation of the head in a male, age 33

occasional flexion at the hip. There may be flexion at the knee joints. Palpation of all muscles in spasm shows them to be of almost stony hardness.

The contraction of the muscles of the lower extremities is so violent that it is difficult to lift them off the bed. The muscles of the abdomen and the accessory muscles of respiration are in extreme tonic contraction. Toward the end of the convulsion there is cyanosis caused by a period of apnea from the tonicity of the muscles of respiration. In males, there may be an expression of prostatic and seminal fluid without an erection. Defecation and urination in bed are frequent occurrences.

The convulsive seizure lasts about one minute, and it is probably the most violent ever recorded in human beings. When the convulsion is over, the patient's color gradually approaches the normal. Consciousness returns quickly or slowly, quietly or accompanied by excitement. The muscles of the jaw seem the last to relax and this relaxation is sometimes not complete for about 15 minutes. The patient may fall into a slumber, the duration

of which as a rule is not more than ten minutes. This is followed by fatigue. About an hour after the therapy, he is allowed up for a bath and breakfast.

Analysis of Statistics—Table II includes injuries complicating the hypoglycemic convulsions of insulin therapy. It will be noted that the total number of patients who suffered injury was 72, of whom 46 were male and 26 female. The oldest patient was 44, the youngest 17 and the average age was 29. The total number of fractures in both the insulin and metrazol therapies was 13 (0.6 per cent), and dislocations, 120 (5.7 per cent). Sixteen of these patients had recurrent dislocations of the mandible, one as many as 14. Twelve fractures (1.78 per cent) and 118 dislocations (17.2 per cent) complicated convulsions from metrazol therapy, and one fracture (0.07 per cent) and two dislocations (0.14 per cent) were produced by complicating hypoglycemic convulsions during insulin therapy. The average duration of a convulsive seizure was about one minute and the largest number of convulsions previous to injury was 33. There are recorded 24 patients injured during the initial convulsion. Eighty-three point seventy-six per cent of the patients had no restraint. The anatomic diagnoses are also designated (Table II).

TABLE II

ANALYSIS OF TABLE I

Number of patients treated with metrazol	687
Number of patients treated with insulin	1,404
Number of males injured	46
Number of females injured	26
Age of oldest patient	44
Age of youngest patient	17
Average age	29
Largest number of convulsions previous to injury	33
Number of cases injured during initial convulsion	24
Average duration of convulsive seizure	1 minute
Percentage with no restraint	83.76

ANATOMIC DIAGNOSES

	Totals
Dislocation mandible*	105
Dislocation head humerus	15
Intracapsular fracture neck femur	3
Intertrochanteric fracture neck femur	2
Fracture greater and lesser tuberosity humerus	1
Fracture greater tuberosity, dislocation head humerus	2
Compression fracture seventh dorsal vertebra	1
Fracture transverse processes fifth lumbar vertebra	1
Fracture neck humerus	1
Fracture anatomic neck humerus, fracture greater tuberosity, posterior dislocation head	1
Fracture angle mandible	1
Total Fractures	13—Total Dislocations
	120

* There were 16 patients who had recurrent dislocations of the mandible as follows: 14, 12, 7, 5, 5, 5, 4, 3, 2, 2, 2, 2, 2, 2, 2, 1. Of this number, one patient had 5 dislocations in 5 convulsions, another 7 dislocations in 7 convulsions, and 2 patients had 2 dislocations in 2 convulsions.

	Number of Fractures	Percentage	Number of Dislocations	Percentage
Metrazol	12	1 78	118	17 2
Insulin	1	0 07	2	0 14
Total fractures and dislocations (metrazol)		130		18 9
Total fractures and dislocations (insulin)		3		0 21
Total fractures and dislocations (both treatments)		133		6 36

TABLE III

MECHANISMS OF THE FRACTURES AND DISLOCATIONS BY MUSCULAR VIOLENCE

Lesion	Mechanism
Intracapsular fracture neck femur	Pull of external rotators (obturator internus and externus, gluteus maximus and minimus, quadratus femoris, pyriformis and gemellus superior and inferior) and abductors of hip, mesially and cephalad (gluteus medius, pyriformis, obturator internus and externus, gemellus superior and inferior) against powerful iliofemoral ligament anteriorly
Intertrochanteric fracture neck femur	Pull of external rotators and abductors of hip mesially and cephalad, against pull of adductor group (adductor magnus, longus and brevis and pectineus)
Fracture greater and lesser tuberosity humerus	Pull of supraspinatus, infraspinatus, teres minor, and subscapularis
Fracture anatomic neck humerus, fracture greater tuberosity, posterior dislocation head	Forceful impaction head in glenoid fossa (for fracture anatomic neck and posterior dislocation) Pull of supraspinatus, infraspinatus and teres minor (for fracture of greater tuberosity)
Fracture angle mandible	Comparative weakness of angle Pull of internal pterygoid and masseter cephalad and anteriorly Pull of mylohyoid and digastric caudad and anteriorly
Compression fracture seventh thoracic vertebra	Sudden, initial forceful flexion of thoracic portion of vertebral column by intense spasm of abdominal recti and external oblique muscles
Fracture transverse processes fifth lumbar vertebra	Pull of erector spinae, multifidus, intertransversalis, longissimus dorsi, psoas, quadratus lumborum
Dislocation head humerus and fracture greater tuberosity	Pull of supraspinatus, infraspinatus and teres minor (for fracture) Pull of pectoralis major, teres major, latissimus dorsi and subscapularis (for dislocation)
Dislocation mandible	Normal anterior glide condyloid process Pull of internal pterygoid, masseter, and temporal muscles, cephalad and anteriorly
Anterior dislocation head humerus	Normal redundant shoulder capsule with comparative weakness antero-inferior portion, with arm in abduction Pull of supraspinatus, infraspinatus and teres minor, posteriorly and mesially Pull of pectoralis major, teres major, latissimus dorsi and subscapularis anteriorly and mesially

Mechanism of the Fractures and Dislocations—It is possible that a constitutional inferiority and in certain cases an osteoporosis produced by disuse, sustained posture, or prolonged undernutrition may be contributory predisposing factors to the production of injuries. It is also possible that supposedly therapeutic doses of metiazol have been too high.

The intense tonic and clonic muscle spasm produces a pathologic incoordination between antagonistic groups of muscles, which by their anatomic attachments and strong lines of pull determine the resulting lesion. It is difficult to know at which particular phase of the convulsive state the fractures and dislocations were produced. It, therefore, becomes very difficult to form a precise concept of the various mechanisms entering into the production of the complicating injuries. Brief summaries of the suggested mechanisms are given in Table III.

Suggestions to Minimize Injuries—Forceful manual restraint or the use of restraining sheets should be minimized. Clearly, an additional counterforce added to an already existing pathologic force has a tendency to increase spasm and this causes a greater likelihood of injury. Pressure by a hand upward against the mandible tends to prevent its dislocation. It is a good plan to hold the upper extremities close to the trunk to prevent dislocation of the shoulder.

SUMMARY

(1) A typical convulsion produced by metiazol therapy for schizophrenia is described.

(2) The muscle spasm is so intense that fractures and dislocations by muscular violence alone occur. By contrast, not a single injury of this type occurred in a series of 7,500 epileptic convulsions.

(3) Seventy-two patients suffered injury, of whom 46 were males and 26 females. The oldest was 44, the youngest 17, average age 29.

(4) In a series of 687 cases treated with metiazol one or more times, there occurred 12 (1.78 per cent) fractures and 118 (17.2 per cent) dislocations. In terms of the total number of convulsions (859) up to the time of injury, the fractures constituted 1.5 per cent and the dislocations 13.9 per cent, respectively.

(5) In a series of 1,404 cases treated with insulin, there were one (0.07 per cent) fracture and two (0.14 per cent) dislocations as a result of complicating hypoglycemic convulsions.

(6) All the injuries included five fractures of the neck of the femur, one fracture of the greater and lesser tuberosity of the humerus, one fracture of the anatomic neck of the humerus and greater tuberosity with posterior dislocation of the head, one fracture of the angle of the mandible, one compression fracture of the seventh thoracic vertebra, one fracture of the transverse processes of the fifth lumbar vertebra, two dislocations of the head of the humerus with fracture of the greater tuberosity, 105 dislocations of the mandible, and 15 dislocations of the head of the humerus. Sixteen patients had recurrent dislocations of the mandible.

(7) One-third of the patients suffered injury during the initial convulsion. On the contrary, other patients had many convulsions previous to injury, and one of them had 33.

(8) The mechanism of the production of the various fractures and dislocations is suggested, together with possible predisposing factors.

(9) Suggestions to minimize injuries are made.

(10) The injuries must be seriously considered in electing to employ metrazol therapy.

Since the writing of this article, there have been three additional cases of fracture of the neck of the femur at the Rockland State Hospital from convulsions produced by metrazol therapy. At the Psychiatric Institute 20 males and 31 females had 529 convulsions as a result of the therapy. Compression fractures of bodies of vertebrae were demonstrated by roentgenogram in a total of 22 (43.1 per cent) of the 51 patients and they included six males (30 per cent) and 16 females (51.6 per cent). All the fractures were found in the thoracic vertebrae, most commonly in the midthoracic region. The number of segments affected varied from one to eight, and the average was between three and four.

REFERENCES

- ¹ Finkelman, Isidore, Steinberg, D. Louis, Liebert, Erich. The Treatment of Schizophrenia with Metrazol by the Production of Convulsions. *JAMA*, 110, 706-709, March 5, 1938.
- ² Nightingale, G. S. Six Months' Experience with Cardiazol Therapy. *Jour. Ment. Sci.*, 84, 574-580, May-July, 1938.
- ³ Dhunibhoy, J. E. Treatment of Schizophrenia by Induced Convulsions. *Lancet*, 1, 370-371, February 12, 1938.
- ⁴ Lebensohn, Zigmund M. The Present Status of the Metrazol Therapy of Schizophrenia. *Med. Ann. District of Columbia*, 7, 33-41, February, 1938.
- ⁵ Sakel, Manfred. Neue Behandlungen der Morphinsucht. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 143, 506-534, January 10, 1933.
- ⁶ Sakel, Manfred. Schizophreniebehandlung mittels Insulin—Hypoglykämie sowie Hypoglykämischer Schocks. *Wien. Med. Wchnschr.*, 84, 1211-1214, November 3, 1934.
- ⁷ Gross-May, Gerty. Über Epileptiforme Anfälle bei der Insulintherapie der Schizophrenie. *Der Nervenarzt*, 11, 400-413, August, 1938.
- ⁸ Nyíró, Gyula, and Jablonsky, A. Nehány adat az Epilepsia prognózisához kulonos tekintettel a constitutióra. *Orvosi Hetilap*, 73², 679-681, 1929.
- ⁹ Müller, Georg. Anfälle bei Schizophrenen Erkrankungen. *Allg. Ztschr. f. Psychiat.*, 93, 235-240, 1930.
- ¹⁰ Glaus, A. Über das Vorkommen von Paralyse bei Schizophrenie. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 132, 151-183, February 6, 1931.
- ¹¹ von Meduna, Ladislaus. Über experimentelle Campherepilepsie. *Arch. f. Psychiat. u. Nervenkr.*, 102, 333-339, September 20, 1934.
- ¹² von Meduna, Ladislaus. Versuche über die biologische Beeinflussung des Ablaufes der Schizophrenie. Campher und Cardiazolkämpfe. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 152, 235-262, February 19, 1935.

THE USE OF VITALLIUM AS A MATERIAL FOR INTERNAL FIXATION OF FRACTURES*

WILLIS C CAMPBELL, M D , AND J S SPEED, M D

MEMPHIS, TENN

ANY discussion of the methods of internal fixation of fractures, necessarily, brings up the whole question of the advisability of treating fractures by open reduction. There is much to be said on both sides. A satisfactory functional result, rather than dramatic roentgenograms, is the prime object in the treatment of every fracture, and the simplest and safest method of obtaining this result is the one to be employed. The majority of fractures can be reduced by manual force and the position of the fragments maintained by external immobilization and traction.

In certain types of fractures, on the other hand, experience has shown that open reduction and some means of internal fixation is the only procedure which offers the patient a reasonable expectation of satisfactory function. The wholesale adoption, by the inexperienced, of the first steel plates used for the internal fixation of fractures was followed by such a deluge of disastrous results that the method, in general, fell into disrepute. This unfortunate situation, however, has led to certain developments in bone surgery which now permit a more aggressive attitude toward those fractures in which serious impairment of function appears inevitable by treatment with conservative measures. The introduction by Doctor Venable of vitallium, an alloy which is practically inert in the tissues, as a means of internal fixation, has been one of the outstanding contributions to our advance in bone surgery.

Vitallium is a nonferrous alloy, being composed of cobalt, chromium and molybdenum. Its physical and chemical properties, and its reaction when placed in living tissue, have been described in articles by Doctors Venable, Stuck and Beach. Experimental and clinical evidence indicate that vitallium is the most "silent" of all the metals or alloys employed for internal fixation of fractures. The most serious objection to other material utilized for this purpose was their electrolytic action upon the host tissue, as manifested by a local area of tissue necrosis, with absorption of the bone about the screws and plate. The consequent loosening of the screws impaired the stability of the internal fixation, and the devitalized tissue favored bacterial growth.

This article is based upon a study of 65 cases in which vitallium was employed in the form of plates or screws, or both, as a material for internal fixation of various types of fractures. The tissue response to the metal was observed for the purpose of determining the presence or absence of (1) Cor-

* Read before the Southern Surgical Association, White Sulphur Springs, W. Va., December 6, 7, 8, 1938.

erosion of the metal with staining or devitalization of the adjacent soft tissue, (2) absorption of the bone about the screws, (3) incidence of infection in simple fresh fractures, (4) tolerance of the tissues to the vitallium in potentially infected compound fractures, and (5) the reaction of both bone and soft tissues to the vitallium in obviously infected compound fractures

If the many disastrous results which have occurred in the past following the adoption of open reduction and internal fixation in the treatment of fractures are to be avoided, scrupulous attention to the principles of surgical asepsis must be observed. Exposure converts a simple fracture into a poten-



FIG 1—(A) Simple fracture of both bones of the forearm treated elsewhere by open reduction and wiring, subsequent nonunion treated by sliding bone graft operation with fixation by steel screws. When first seen by the author patient had active infection in the operative wound, there was absorption of bone about the screws, and the grafts had sequestered. (B) Same fracture showing condition following removal of sequestra. Resulting scars the soft tissue infection and bony defects prevented any reconstructive surgery indefinitely. This surgical disaster may accompany any open reduction of fractures.

tially compound fracture, with all of its attendant risks. Under proper conditions, these risks are not serious and are far outweighed by the advantages of accurate replacement of the fragments and secure fixation.

Skin Preparation and Protection—The practice of shaving and cleansing the skin on the operating table immediately prior to operation is to be avoided whenever possible. Rather, a preliminary preparation, consisting of shaving and thorough washing with soap and water, followed by the application of benzine, ether, and the routine skin antiseptics, and a sterile dressing should be made 12 hours before operation. A second routine preparation is carried out on the table. During operation, contact with the skin is avoided by

enclosure of the member in sterile stockinette fastened to the skin edges of the wound

Operation should never be undertaken immediately after removal of a plaster encasement. The region which has been enclosed in the encasement is covered with partially desquamated skin which cannot be removed during the ordinary surgical preparation. A period of at least four days should be allowed for adequate cleansing of the skin.

A routine method of draping the extremities, which provides protection against contamination of the hands during the draping and of the operative field during movement of the extremity incident to reduction of the fracture, should be mastered by the entire surgical team. This admonition perhaps seems unnecessary, but the authors have observed that, in many hospitals, in which the majority of the surgery is abdominal, both the operative field and the hands of the surgeons are often contaminated during the draping of an extremity, before the operation is begun. Again, unsterile fields are frequently exposed at operation by the movement of the extremity necessary in the procedure.

Instrumental technic has many advantages and should be employed when possible, but is impracticable unless the entire operating team works together routinely and is trained in the details of technic. The chief advantage of instrumental technic is the avoidance of gross tears or small puncture openings in the gloves of the surgeon, through which perspiration may escape into the wound.

USE OF VITALLIUM IN ACUTE FRACTURES

Acute fractures in which internal fixation is indicated may be divided into two groups.

(1) *Fractures of Necessity*. This group includes those types of fractures in which experience has shown that satisfactory position of the fragments cannot be secured or maintained by manual force or skeletal traction, and those in which treatment by these methods has failed to achieve an alignment of the fragments adequate to prevent serious disability or deformity.

(2) *Fractures of Election*. In this group, although sufficient anatomic position has been or can be obtained by closed reduction to afford a good functional result, the degree of displacement warrants the expectation of some deformity, a slow union, and a slight permanent disturbance in function. Formerly, this condition would have been preferable to the risks attendant upon open reduction and plating. The negligible danger incident to internal fixation with vitallium and the probability of obtaining a better functional result with a shorter period of disability, justifies a more aggressive attitude toward this type of fracture.

There is a third group of acute fractures in which the question arises as to whether internal fixation or skeletal traction should be employed. The

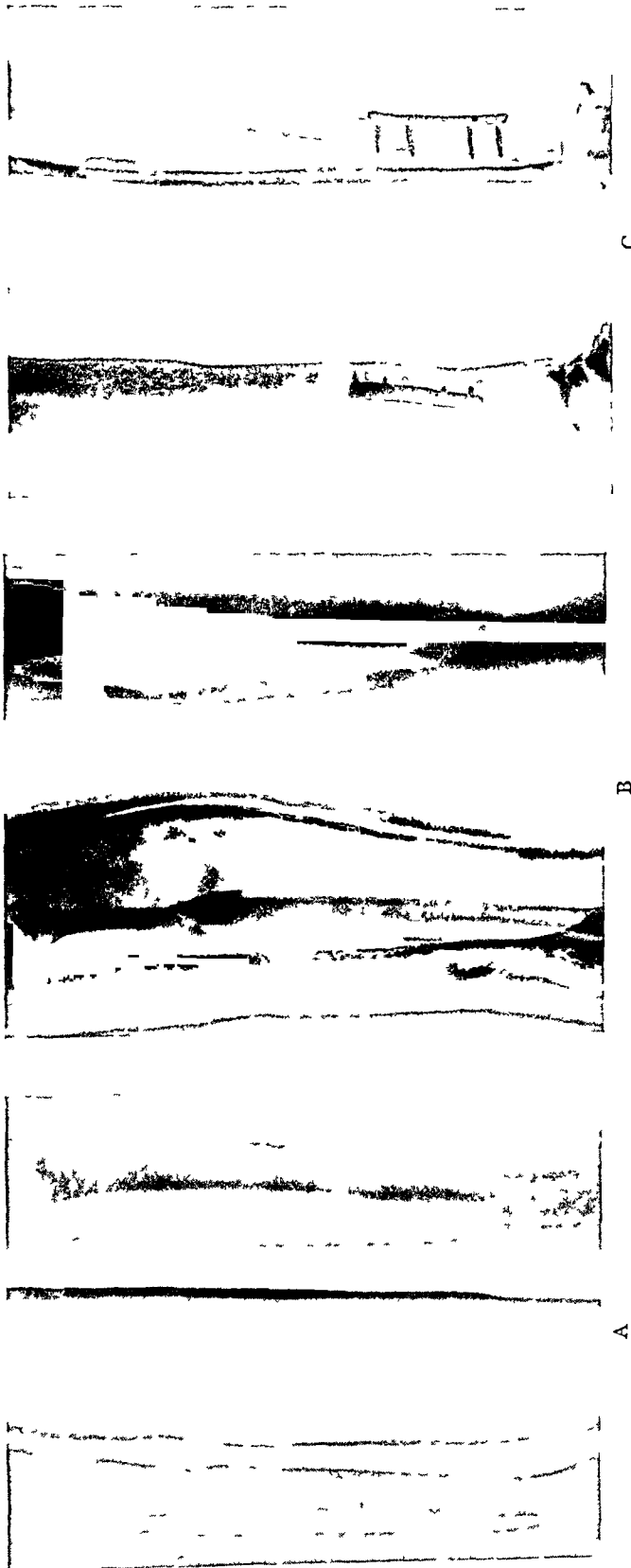


FIG 2—(A) Comminuted oblique fracture of the tibia and fibula. Roentgenogram made after closed reduction and application of plaster encasement shows satisfactory reduction. (B) Roentgenogram made through encasement showing displacement of fragments, sufficient to delay union and impair function slightly. (C) Same fracture two months after open reduction and internal fixation with vitallium plate. Solid bony union with restoration of normal anatomic position. This is a borderline case in which deformity would have been accepted before present methods of open reduction and plating were adopted.

choice here will depend upon the experience of the operator, the surgical facilities available, the general condition of the patient, and the local condition. Skeletal traction obviates the danger of wound infection and involves less surgery, but does not insure anatomic precision in the restoration of the position of the fragments. Further, longer periods of immobilization and hospitalization are required for skeletal traction. In the presence of infected skin lacerations or "brush burns" adjacent to the operative field, however, there is danger of operative infection, and accuracy of reduction should be sacrificed in favor of the safer method of skeletal traction.

Vitallium has been employed routinely by the authors as a material for internal fixation only during the past year. Twenty-two acute simple fractures have been plated, and from a clinical standpoint the method has, unquestionably, proved superior to anything we have employed previously. In some cases, roentgenograms have been made at intervals over a period of 10 months. There has been no evidence of absorption of the bone about the screws, nor any inflammatory changes in the soft tissues. The metal seems entirely inert and silent. In many cases, callus appears to have covered the plate partially—a feature seldom observed following the use of plates composed of ferrous alloys.

The majority of patients have no symptoms from the plates, and do not wish to have them disturbed. We have, however, removed eight plates which had remained in the tissues from four to 10 months. These did not show any evidence of corrosion or tarnishing. The screws were firmly imbedded in the bone, and had to be freed with a screwdriver. In no case, even in frankly infected compound wounds, were we able to lift the screws out with a hemostat, as is often possible when screws of ferrous alloys are used. The soft tissue about the plates was not stained, and appeared to be normal scar and fibrous tissue, similar to that formed in the healing of any surgical wound. In two cases, it was necessary to resect callus from over the plate before its withdrawal.

Complete immobilization and alignment of the fragments have been maintained in all cases with the exception of one, in which the plate broke. This plate was under considerable tension in the upper end of the femur and was, moreover, one of the earlier types manufactured, in which the alloy was rather brittle. This brittleness has since been corrected, and the plates are now sufficiently malleable to bend slightly to fit the contour of the bone and obviate the danger of breaking.

In the group of acute clean fractures, three infections have developed. Violation of the rules which govern operation was directly responsible for the infection in two of the three cases. In one, the operation was performed immediately after removal of a plaster encasement which had been worn for several weeks. Proper skin preparation was impossible. In the second case, there were "brush burns" adjacent to the operative site. Both of these infections could have been avoided by proper selection and preparation of the cases.

Union has taken place in all of the acute fractures. Even in the three cases in which infection developed, the fragments eventually united in satisfactory position. In the infected cases, it was necessary to remove the plates before all drainage ceased.

USE OF VITALLIUM FOR DELAYED UNION OR MALUNION OF FRACTURES

Vitallium plates have been applied to 12 fractures in which union was delayed and the fragments were in malposition, or following osteotomies for malunited fractures. In delayed union with malposition, freshening of the

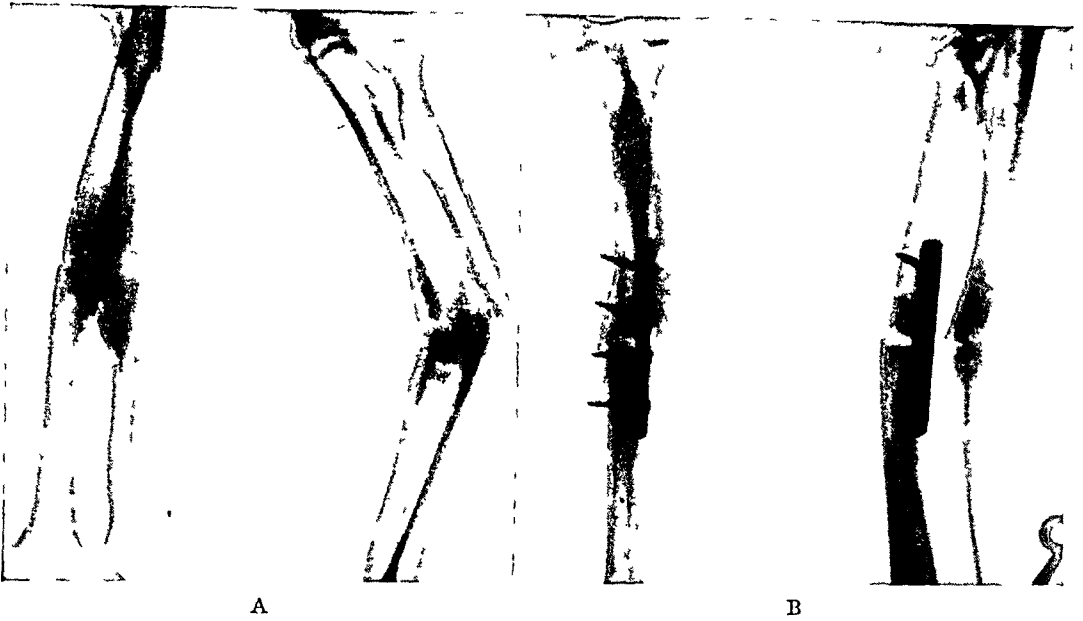


FIG. 3.—(A) Malunion of both bones of the forearm. The ends of the fragments are sclerotic and the bone is of poor quality for callus production. In this type of case a bone graft is preferable to plating. (B) Vitallium plate was applied to radius. Union was not solid after five months, union in both fractures solid ten months postoperatively. Fracture of radius united before that of the ulna.

ends of the fragments, realignment, and secure fixation by means of a vitallium plate are usually sufficient to insure union. Fixation by the plate prevents recurrence of the displacement, which is not unlikely when union is delayed. Elimination of all movement between the fragments promotes earlier union.

In several fractures of both bones of the forearm, where one bone was plated and the other merely freshened and realigned, solid union took place in the plated earlier than in the unplated bone.

Vitallium plates are indicated as a means of fixation in malunited fractures after correction of the deformity, provided the quality of the bone is good and normal callus production may be anticipated. If the ends of the bone are sclerotic and of poor quality, and callus production will probably be slow or inadequate, an autogenous bone graft is preferable, since it affords not only mechanical fixation, but also a stimulus to osteogenesis, which is necessary in this type. Convincing evidence of this fact has been observed in three cases.

of malunion in which osteotomies were carried out and vitallium plates were applied for fixation. The bone was somewhat sclerotic in all these cases and union was delayed over a long period of time, being questionable at the end of seven months in one case and after 10 months in another. In one or two other cases definite roentgenographic demonstration of solid bony union was not present for many months. Although union ultimately became solid in all these fractures, the period of disability would no doubt have been shortened and union made more certain by the use of a bone graft.

There were no infections in this group, and the roentgenograms revealed

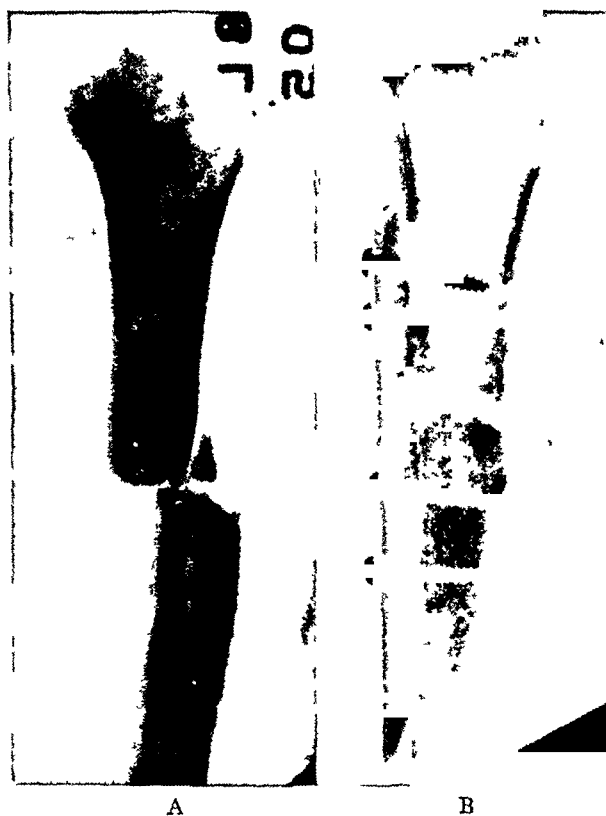


FIG 4—(A) Nonunion of fracture of the humerus of four months' duration. (B) Roentgenogram three and one half months postoperatively shows solid union after fixation by only bone graft and four vitallium screws.

no absorption about the screws. Thus far, the plates have not been removed in any of these cases.

USE OF VITALLIUM IN UNUNITED FRACTURES

Surgical procedures to induce bony union in typical ununited fractures must fulfill two fundamental requirements to insure the highest percentage of successful results: (1) Accurate reduction, and adequate fixation to prevent motion between the fragments; (2) stimulation of osteogenesis.

In many ununited fractures the ends of the fragments are sclerotic, the blood supply poor, and there are other conditions unfavorable for the reformation of callus. Every possible stimulus to the formation of new bone should

be provided. For these reasons, it is felt that the use of vitallium plates should not be extended to replace bone grafts in typical nonunion. Although removal of intervening scar tissue, freshening of the ends of the fragments, accurate reduction, and complete fixation by metal plates will induce bony union in many cases, this method is less likely to be successful than fixation by bone grafts.

Solid bony union has been obtained in 93 per cent of our series of over 400 bone grafts for nonunion of fractures. We have not applied vitallium plates in typical ununited fractures, but have used vitallium screws, either alone or in combination with autogenous bone nails, as a means of fixation of these bone grafts. The use of vitallium screws simplifies the operative procedure and provides firmer fixation for the grafts than autogenous bone nails. In none of the 19 cases in which screws have been used, have any deleterious effects been observed.

USE OF VITALLIUM IN ACUTE COMPOUND FRACTURES

Sherman and others have employed metallic plates in the treatment of compound fractures for many years, and have reported excellent results. Following the use of ferrous alloy plates, the majority of surgeons have found the incidence of infection with loosening of the screws and loss of position resulting from instability of the plate relatively high. For this reason, foreign materials for internal fixation in compound fractures have been utilized with some hesitancy. The immediate accurate reduction and secure fixation of the bony fragments in compound fractures, however, has several advantages. First, these fractures are more easily reduced immediately following injury than at any time afterward. Second, accurate reduction unquestionably hastens union. Obliteration of dead space and pockets about the ends of the bones diminishes the likelihood of infection. Third, with internal fixation there is need for less external immobilization, thus permitting observation and treatment of the damaged soft parts without constant movement at the fracture site—a disadvantage of skeletal traction.

The clinical demonstration that vitallium plates are relatively inert in the tissues, apparently having no unfavorable influence upon the incidence of infection, and the fact that there is no absorption about the screws even in the presence of infection, has convinced us that the advantages of its use in connection with compound fractures usually outweighs any theoretical objection.

The following routine technic has been adopted for the treatment of acute compound fractures.

GROUP I—*Acute compound fractures seen during the first 12 hours after injury, in which the fracture has been compounded from the inside or there is relatively little damage to the soft tissues.* Under general anesthesia, the skin of the extremity is thoroughly cleansed with soap and water and prepared as for any operation. All obviously devitalized tissue is removed from the wound by débridement. The wound is then cleansed mechanically by copious irriga-

tion with normal saline solution, no strong antiseptics are used in the open wound. The fracture is next exposed, reduced, and immobilized with a vitallium plate and screws. The wound is partially closed, and a plaster encasement or splint applied. The administration of sulfanilamide is begun at once, as a prophylaxis against infection.

GROUP II—*Compound fractures seen after 12 hours, or those in which there is extensive damage to the soft tissues.* In these cases, the above procedure is carried out and, in addition, incisions are made at optional points for counter drainage and the insertion of Dakin's tubes. Routine Dakin treatment is then instituted, and whatever type of external immobilization appears most suitable is applied.

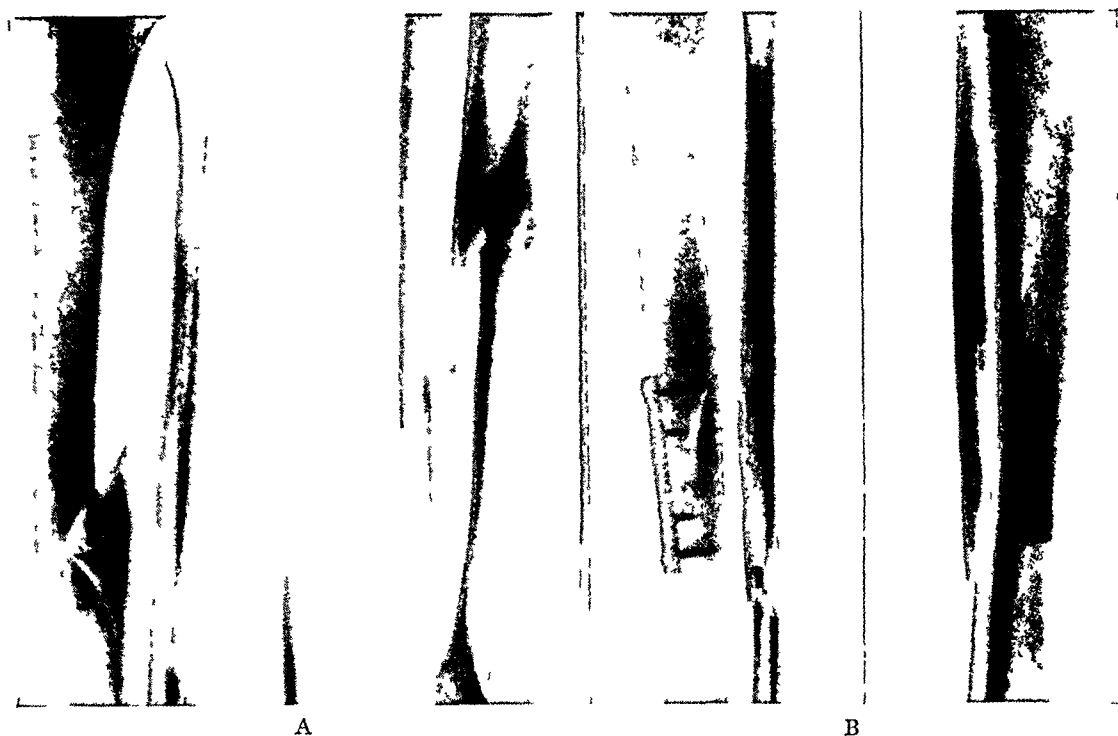


FIG 5—(A) Acute compound fracture. (B) Same fracture after open reduction and application of vitallium plate. Wound healed without infection. Solid bony union two months after operation.

In some cases, skeletal traction is combined with these procedures.

In fractures of the tibia and fibula or radius and ulna, in which the fracture is compound in one bone and simple in the other, open reduction and internal fixation of the simple fracture will frequently maintain alignment of both bones and obviate the necessity of operating upon the compound fracture. Fixation of the fibula in compound fractures of the tibia is a typical example of this variation from the usual operative procedure.

Eight of the fractures of our series were in GROUP I. All wounds have healed primarily, there has been no infection, and the plates are still *in situ* in every case. In the fractures of GROUP II, in which the wounds were grossly contaminated, there have been, of course, mild infections, these have been controlled with Dakin treatment. In no case has a severe, extensive

infection developed. The plates have maintained satisfactory position of the fragments, and the screws have not been loosened even in the presence of infection. In the majority of grossly infected cases, removal of the plate has been necessary before drainage ceased.

Although our group of compound fractures treated by fixation with vitallium plates is as yet too small to justify any positive conclusions, the clinical results following the above method of treatment have been so successful that we feel further experience will prove its soundness, and the morbidity and period of disability will be reduced. Further, the time of observation is too short to permit conclusions in regard to the rapidity of union as compared to that following treatment by skeletal traction. Apparently, however, the plate does not in any way interfere with the process of callus formation, and

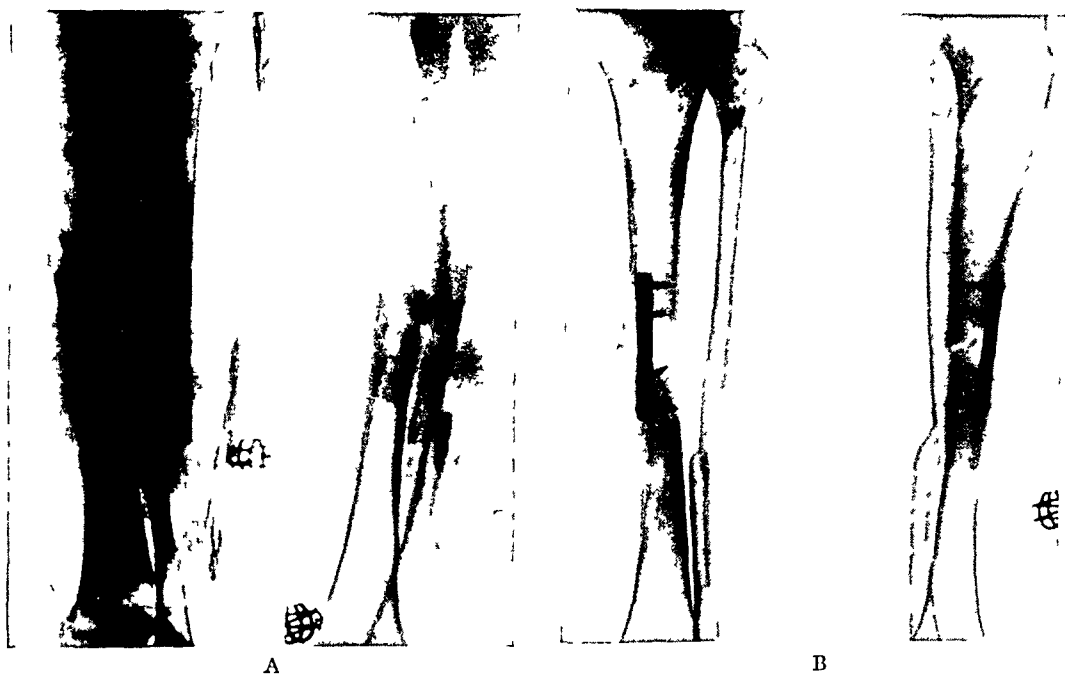


FIG. 6—(A) Infected compound fracture of two months duration, treated by skeletal traction in plaster encasement, resultant malposition and nonunion. Correction impossible by manual force or traction. (B) Condition five months after correction and fixation by vitallium plate through infected field. Position is maintained, no osteomyelitis. No absorption about screws despite infection. Union practically solid.

maintenance of position with lack of movement between the fragments shortens the time required for union.

USE OF VITALLIUM PLATES FOLLOWING CORRECTION OF DEFORMITY IN OLD INFECTED COMPOUND FRACTURES

Encouraged by the results which we have obtained in the group of acute compound fractures, we have in a few cases undertaken the correction of malpositions in old infected compound fractures with persistent drainage.

Since the operation is of necessity carried out through an infected field sulfanilamide is given several days previously. We have been impressed with

the apparent value of this drug as a prophylactic measure in acute compound fractures and in reconstructive operations in which reactivation of an old infection appears probable

In order to minimize the danger of sequestration of the ends of the fragments resulting from disturbance of the blood supply by the mobilization necessary to reduction, stripping of the periosteum and soft tissues from about the fragments should be restricted so far as possible. In compound fractures in malposition, nonunion is common, and union is always delayed. Gross deformity and serious disturbance in function are inevitable.

CONCLUSIONS

Vitallium was first used in the manufacture of dentures, where resistance to infection and corroding secretions was essential. Its negligible electrolytic action, as proved by the lack of inflammation in the tissues about these plates, and the absence of absorption of bone about the screws, has made vitallium a dependable material for the fixation of fractures even in the presence of gross infection. It is not contended that the use of vitallium for internal fixation in infected compound fractures will prevent the spread of infection or the sequestration of devitalized portions of bone. Both experimental and clinical evidence, however, indicate that vitallium will aid in reducing these complications to a minimum, and that the screws will hold the plate firmly in position, preventing displacement of the bone fragments until union is firm.

DISCUSSION —DR CHARLES VENABLE (San Antonio, Texas) I cannot express to you how gratifying it is to see what I hoped would be true, especially as Doctor Speed and Doctor Campbell have always been opposed to hardware. I agree entirely with what Doctor Speed has to say about the selection of cases, in old ununited fractures in which the bone ends are ebonized, I think the bone graft is preferable. I feel the field is open. Indeed, we have introduced vitallium caps in cases of ankylosed hips, with gratifying success, and hope, with the experience of others gradually taking up this procedure, we may find in the course of time that we may save not only time, but may lessen the postoperative disability in arthroplasties, also that we have simplified the procedure and put it in a field that may lead to many more.

DR EDGAR L. GILCREEST (San Francisco, Calif.) I believe that the introduction by Doctor Venable of vitallium in the treatment of fractures is epoch-making. It is the first metallic substance we have ever used for the internal fixation of fractures which is nonirritating. The toleration of vitallium by the bone and the surrounding tissues, as shown so clearly by Doctor Venable's experimental and clinical experience and by the interesting group of cases of Doctors Campbell and Speed, leaves no doubt that this metal will be used more and more. I admit that it does give the surgeon a feeling of assurance that he never had before, which could be compared to the cool confidence the Christian has who holds four aces!

It is here, however, that the danger lies, and that a note of warning should be sounded. Because it is nonirritating it will be used too often when not indicated. Always the pendulum swings too far, human nature running true to form. We should remember that the basic and fundamental principle in

the treatment of fractures does not change and that is that all fractures, if possible, should be treated immediately by a nonoperative method. In 1922, I read a paper before this Association emphasizing this point, and through the years since then I have become more convinced than ever of the soundness of this view. I hope, therefore, that the unwarranted use of this very valuable metal, for which the profession is indebted to Doctor Venable, will not bring it into disrepute which, unfortunately, so often happens.

DR J S SPEED (Memphis, Tenn., in closing) I would like to emphasize again that the method of open reduction of fractures and the use of internal fixation should be undertaken with great caution, to avoid the many serious complications which accompanied the original adoption of the older Lane's plates. The operation is not a minor procedure, and should be performed under the most rigid conditions of surgical asepsis. The use of vitallium plates in connection with fresh or old compound fractures must be guided by that judgment which comes from experience in handling these cases.

BRIEF COMMUNICATIONS

ARTERIOVENOUS ANEURYSM OF THE NECK, UNTREATED*

JOHN M. HANFORD, M.D.

NEW YORK, N. Y.

Case Report.—A female, age 35, presented herself at the Vanderbilt Clinic in November, 1934, complaining of a lump in the left side of the neck of nine years' duration. She had first noticed this three months after a confinement, when it grew rapidly for a few weeks. Since that time it had grown slowly. In 1931, a separate small nodule was noticed. The swelling was unaccompanied by pain or tenderness. She has four children, living and well, and has had three miscarriages. Tonsillectomy was performed in 1922, prior to which she had had tonsillitis. In 1923, she was said to have had "sprue," of which no symptoms remained. There was an abscessed tooth in 1931. Otherwise her past history was negative. She has had no upper respiratory infection or loss of weight. However, she had been in contact with her mother who died of tuberculosis.

Physical Examination.—There is a hard, nontender mass, 8 by 5 cm. in size, on the left side of the neck, beneath the sternocleidomastoid muscle, which is movable laterally but not vertically. A definite systolic thrill and bruit are observed over the swelling. Below this is a smaller nodule, about 1 by 2 cm. in size. The isthmus of the thyroid gland appears nodular and there is a nodule on the right. The trachea feels displaced slightly to the right. There is a bruit also over the right carotid artery. It has been noted that the bruit could be obliterated by compression of the lower part of the left common carotid artery. Except for diminished resonance over the right apex, other examination is negative. The bruit is heard as continuous—never ceasing.

Laboratory and Roentgenologic Data.—Wassermann negative. Hemoglobin 68 per cent. Red blood cells 4,400,000. White blood cells 8,200, polymorphonuclears 53 per cent, small lymphocytes 41 per cent, large lymphocytes 5 per cent, eosinophiles 1 per cent. The urine shows a faint trace of albumen, many pus cells, moderate epithelial cells. Roentgenologic examination of the chest shows peribronchial thickening in both upper lobes, with scattered semicalcified lesions at both apices. There is thickening of the overlying pleura. Nothing is seen which can be interpreted as fresh infiltration. A film of the cervical soft tissues shows no evidence of calcification.

This is thought to be a remarkable case of apparently nontraumatic or congenital arteriovenous communication in the left side of the neck. There are also nodules in the left side which are thought to be unrelated to the aneurysm and which are considered to be possibly tuberculous lymph nodes or lateral aberrant thyroid nodules, as the lower ones appear to be close to the thyroid gland. After compressing the left common carotid for only half a minute, the patient felt dizzy and noticed numbness in her right arm.

In December, 1934, aspiration over the site of the bruit on the left yielded 5 cc. of blood, intermediate in color between arterial and venous. Roentgenologic examination of the neck following "skiodan" injection showed "Two films are of some aid in diagnosis out of a total of seven. Apparently the 'skiodan' injected into the mass in the cervical region has outlined, at least partially, an aneurysm sac, together with a tortuous vessel, lying medial to and above it, and one lying more lateral and posterior to

* Presented before the New York Surgical Society, April 13, 1938. Submitted for publication May 31, 1938.

it These I would judge to represent the artery and the vein It looks as though a clot may be displacing the 'skiodan' within the aneurysm" (Dr Swenson) A roentgenogram of the heart showed "The measurements, at two meters, are MR 23 ML 74 TD 97 GV 52 Internal diameter of the chest 240 This shows no abnormality of the cardiac contour or size The old minimal calcified tuberculous lesions in the apices are noted" (Dr Abbott)

The patient was urged to practice compression on the left carotid artery daily and was sent home, to return later for operation, if found necessary after subsequent examination

She has been seen off and on in the clinic since then Shortly after leaving the hospital, it was found that she could stand compression for a longer period than when she left She apparently did not practice the compression as often as we wished, due to lack of time In January, 1935, I was impressed with the remarkable decrease in the neck swelling (*i e*, the aneurysm) during compression below

In April, 1935, there had been no advance of the neck disease and the patient presented no evidence of cardiovascular damage At that time, I felt inclined toward the diagnosis of lateral aberrant thyroid nodules with a coincident vascular anomaly in the form of an arteriovenous communication, and advised against operation for the time being Three months later, I felt inclined to the diagnosis of lateral aberrant thyroid nodules, nontoxic nodular goiter, and congenital arteriovenous aneurysm In November, 1935, my note reads "No change I am even more inclined to the diagnosis of nontoxic adenoma of left lobe of the thyroid gland, of aberrant thyroid nodules, and of congenital arteriovenous fistula"

Since then the patient has been seen every two or three months until the present time (1938) She has had several colds, sleeps poorly, and is continuously overtired, apart from which there has been no essential change in her neck or general condition since she was first seen by us in November, 1934 In view of this, operation has been postponed indefinitely

COMMENT—It is possible that the firm mass felt in the neck is a thrombosed or partially thrombosed (and by now probably organized) aneurysmal sac This theory is supported by the roentgenologic study with "skiodan" During a period of three and one-half years of observation, with a total history now of twelve and one-half years of swelling in the neck, it does not appear probable that the fistula will cause harm The nodules, however, especially if aberrant thyroid nodules, may become malignant and perhaps for this reason operative removal is advisable

DISCUSSION—DR WM DEW ANDRUS (New York) felt that the audible murmur would certainly seem to be of the type one would expect to find in an arteriovenous aneurysm However, it lacks one sign distinctly characteristic of abnormal arteriovenous communications of the duration of this patient's lesion, namely, dilatation of the surrounding veins In the two cases of abnormal arteriovenous aneurysm of the neck seen by Doctor Andrus, both congenital, the dilatation of the veins of the neck was a striking feature In this particular case, he felt that diagnosis rests between an arteriovenous communication and a simple aneurysm, possibly here associated with some clotted blood or partial clotting in the sac Also, although distinctly more rare than the aneurysm, one must consider a carotid body tumor, very vascular in nature

Doctor Andrus cited a case in which he performed a proximal ligation for what was felt to be a carotid aneurysm and which was characterized by

an expansile pulsation, and a murmur not nearly as loud or rough as this or quite so continuous. The patient died 10 months after operation, and at postmortem examination, was found to have a very vascular carotid body tumor. So far as the surgical attack on this case is concerned, since the mass has not enlarged in the past two or three years, one might be tempted not to operate for the time being, but Doctor Andrus felt it would probably be necessary to operate eventually. If it should prove to be an arteriovenous aneurysm, double ligation and division of the canal of communication would be the ideal procedure, but if this is not possible, quadruple ligation with excision of the fistula-bearing portion of the vessels should be attempted. In aneurysms of this region Doctor Andrus said he prefers to ligate the external carotid and put an aluminum band on the common carotid. If any evidence of cerebral anemia supervenes, the band can be removed—making the obliteration temporary.

DR JOHN M. HANFORD (closing). In this patient, the roentgenograms showed a cavity, and when the "skiodan" was injected, there was a definite space with some dilatation, apparently. It was thought that the needle was in a vascular space because semidark blood, that looked like a mixture of arteriovenous blood, was obtained. This would seem to indicate that there was a cavity, and argue against a carotid body tumor. It is possible that the lesion is a simple aneurysm, but it does have the characteristics of an arteriovenous type of lesion.

ANEURYSM OF THE EXTERNAL CAROTID ARTERY WITH CAROTID SINUS REFLEX

Case Report—A male, age 50, presented himself at the Vanderbilt Clinic in March, 1936, complaining of a small lump in the right side of the neck of about eight months' duration. Eighteen months prior to this, while stoking a boiler, he felt a sudden sharp pain in the right side of the neck, below the mandible, in the region of the present lump. He became dizzy and had a choking sensation, but did not collapse, he had to lie down and rest. He was conscious of a throbbing pain in the neck and temples, which gradually abated. After that time he had frequent similar episodes, which came on chiefly at night without apparent cause. He had had some precordial pain and slight dyspnea during this period. With these transitory attacks he also had dizziness, pain in the temples and right side of the neck, and flushing of the face and neck, mostly on the right side. He had not noticed that local pressure induced an attack.

His past history was essentially irrelevant. He had had attacks of malaria while on military service in India, Africa, etc. (1906-1919), and had had a bilateral ligation performed for varicose veins in 1930.

Physical Examination—A generally healthy man presented a pulsating mass, about 2.5 cm. in diameter, just in front of the carotid bulb in the right side of the neck at the level of the upper border of the thyroid cartilage. The face and neck were somewhat flushed, though not markedly. Compression of the common carotid artery in the lower part of the neck obliterated the swelling and almost obliterated the pulsation. Pressure upon the mass produced no symptoms, except that it was slightly tender. The general examination revealed a slightly enlarged heart and a blood pressure of 145/90. Complete neurologic and ophthalmologic examinations were normal. The Wassermann was negative. Blood count essentially normal. Roentgenograms of the chest and neck showed no abnormality. There was a slight widening of the heart shadow. Blood urea

nitrogen, 17 mg per 100 cc Pulse, 72 *Preoperative Diagnosis* Small aneurysm of the facial or external maxillary artery

Operation—April 30, 1936 Under local anesthesia, through a small, obliquely horizontal incision, the carotid bulb was exposed and a small, cylindrical dilatation of the first part of the external carotid artery found. The carotid bulb itself was normal. The cylindrical dilatation measured about 1 cm in diameter and 2 cm in length. A No. 1 "Deknatel" silk ligature was tied about the proximal portion of the external carotid artery, and a similar one about the origin of the superior thyroid artery, and a third one about the external carotid just above the aneurysm. The artery was not divided. Small vessels were ligated with fine black silk and the wound closed in two layers with fine silk.

Subsequent Course—After a satisfactory postoperative course, the patient left the hospital on the third day, and when seen two weeks later felt "100 per cent better," and no longer felt the throbbing or the dizziness. His face was less ruddy and he had no pain.

He returned for occasional examination. In May, 1937, about one year after the operation, he felt a sense of swelling in the throat and noticed a rash over his neck, shoulders and upper chest. He again had a thorough study in the Medical Clinic, including a roentgenologic study of the chest, and a basal metabolism test. The only significant finding was a somewhat higher blood pressure. In February, 1938, 22 months following operation, the neck presented a definite prominence of the carotid bulb, which had not been present before the operation, but no symptoms developed when the bulb was pressed upon. Blood pressure, 164/100. The chief complaint was the diffuse redness of the neck and upper chest, which was passed upon by the Dermatology Clinic, with the conclusion that the redness was an erythema due to some vasomotor disturbance.

During a recent study in the Medical Clinic, Doctor Southworth suggested that this patient might have a sensitive carotid sinus reflex and, although the clinical picture is not typical of this condition, it is very possible that this case is an example of a sensitive carotid sinus reflex, induced, perhaps, by the dilatation of the external carotid artery, which acted as a local abnormal condition to produce the picture. The typical symptoms, not all present in every case, are: Transitory pallor followed by flushing of the face and neck, fainting, dizziness, convulsions, a fall in blood pressure and slowing of the heart. These symptoms, characteristically, are caused by direct pressure on the carotid sinus or bulb, but also are known to occur spontaneously.

The presumption is that the operation relieved the patient temporarily, but that he developed symptoms later, due to sensitive carotid sinus reflex associated with advancing cardiovascular disease. Since the operation, he has not had dizziness. The benefit derived from the operation may be attributed to the elimination of the aneurysm as a source of pressure, or to a partial denervation of the carotids at the bifurcation.

From a study of the researches of Weiss and his co-workers,^{1 2} the following observations have been abstracted for the purpose of adding to the interest of this clinical presentation. The carotid sinus is the same thing as the carotid bulb, or the normal dilated portion of the common carotid just at and below its bifurcation. The carotid sinus and probably also the adjacent parts of the internal and external carotid arteries are richly supplied with sensory receptors terminating in characteristic menisci. These menisci, par-

ticularly rich in the adventitia, emerge from the vessels as spiral fibers and leave the vessels as the carotid sinus nerve of Hering, or the intercarotid nerve of de Castio. This nerve (or nerves) joins the glossopharyngeal nerve and probably others, including the sympathetic. There is thus formed an afferent, direct connection with the medullary centers.

A small number of persons have a sensitive or hyperactive carotid sinus reflex. A local pathologic condition, it would appear, may induce such sensitivity, or increase the degree of sensitivity in a patient already sensitive. The response to pressure upon the sinus, generally speaking, is greater in persons with hypertension, and still greater in persons with arteriosclerosis.

REFERENCES

- ¹ Weiss, Soma, and Baker, Jas. P. The Carotid Sinus Reflex in Health and Disease. Its Rôle in the Causation of Fainting and Convulsions. *Medicine*, 12, 297-353, 1933.
- ² Ferris, E. B., Jr., Capps, R. B., and Weiss, Soma. Carotid Sinus Syncope and Its Bearing on the Mechanism of the Unconscious State and Convulsions. *Medicine*, 14, 377-456, 1935.

DISCUSSION.—DR. BEVERLEY C. SMITH (New York) remarked that the symptomatology of the case presented is of particular interest in view of the pathology and its site. Clinically the patient showed symptoms of an hyperactive carotid sinus reflex. The carotid sinus plexus derives afferent fibers from the ganglion nodosum of the vagus and the glossopharyngeal nerves. These terminate in sensory end-organs in the wall of the carotid bulb. Afferent fibers are derived from the superior cervical sympathetic ganglion. These are postganglionic fibers and follow the external carotid and middle meningeal arteries, innervating the meninges, and their stimulation produces meningeal and cerebral vasoconstriction and transient pain. Hering and Heymans recently established that the carotid sinus is an important secondary mechanism controlling cardiovascular and respiratory activity. They showed that it plays a part in the regulation of blood pressure, in that, in normal arterial pressure an elevation in pressure in the carotid bulb of 10 to 20 Mm. of water produces marked fluctuation in the systemic blood pressure. Increased carotid sinus pressure causes a lowering in the systemic pressure, and with pressures above 200 Mm. of mercury, and below 50 Mm. of mercury, the reflex control and vasomotor tone disappear. The fall in the systemic blood pressure, following increase in the carotid blood pressure, was accompanied by increase in the size of the spleen and intestines, a diminished rate of blood flow and increase in cardiac volume. Perfusion of the carotid sinus with blood containing varying concentrations of CO₂ and other weak acids accelerated respiration. Perfusion of the isolated sinus, with adrenalin, changes the rate and force of the heart beat. Bronk (1931), using a string galvanometer attached to the sinus and a vacuum tube amplifier, showed that a burst of nerve impulses accompanied each cardiac cycle which was coincident with a rise in the carotid pressure. This action of the sinus was similar to that of the depressor cardiac nerve and tended to prevent high blood pressure or very rapid heart beat.

Weiss and Baker (1934) described a syndrome and recurrent syncopal attacks which they attributed to an overactive carotid sinus reflex. They described fainting, and convulsions from cerebral anemia following this stimulation. In their case, digital compression of the carotid bulb induced similar symptoms to those of the patient's spontaneous attacks.

The following types of reflexes from stimulation of an overactive carotid sinus have been described

(1) Asystole or sudden pulse slowing with or without a fall in blood pressure

(2) A fall in blood pressure, without cardiac slowing

(3) Fainting and convulsions, without marked alteration in heart beat or blood pressure

(4) Complete heart block, temporary ventricular asystole with auricular contraction, nodal rhythm, ventricular extrasystoles, changes in the electrocardiographic T-wave, and complete inversion of the electrical axis of the heart

The efferent arc of this reflex, which was over the vagus, can be blocked with atropin. Novocainization or resection of the sinus nerves prevents the drop of blood pressure, fainting and convulsions following its stimulation.

Periaarterial sympathectomy of the common carotid bifurcation as well as of the lower portions of the carotid arteries have relieved the symptoms of overactive sinus.

White has reported, from Massachusetts General Hospital, a group of cases with this syndrome, treated by periaarterial sympathectomy, and in one of these cases, with a systemic blood pressure of 200 Mm. of mercury, digital compression of the carotid bulb produced a fall of blood pressure to 140 Mm., and a drop in pulse rate from 100 to 60. No electrocardiographic changes occurred. Sustained pressure over the carotid bulb caused deep flushing of face and pain in the arms of the compressed side, and after 20 minutes the patient lost consciousness and had a left-sided convulsion. Following novocaine injection of the carotid bulb sinus region, the symptoms could not be reproduced by the same pressure. His patient was relieved of symptoms by a periaarterial sympathectomy.

The case presented is one of an aneurysm at the origin of the external carotid artery, which involved the fibers of the sympathetic nerves of the bulb region. The patient's dizziness, precordial pain, slight dyspnea, pain in his temples and right side of the neck, and flushing of his face as well as the induction of these symptoms by pressure over the carotid, have ceased since the ligation of the aneurysm.

MALIGNANT HEMANGIO-ENDOTHELIOMA OF THE NECK

Case Report—A male, age 25, presented himself at the Vanderbilt Clinic in October, 1937, complaining of a "growth at the base of the neck." He stated that about two years prior to this he first noticed a firm, nontender lump, the size of a marble, in the right supraclavicular region of the neck and, until about three months ago, this had not troubled him in the least. At that time he was suddenly seized with a dull aching pain in the right shoulder, which radiated down his right arm. This pain persisted for about three weeks and was accentuated by motion in the shoulder joint. By this time the lump had increased in size, so he said, to approximately that of a tennis ball.

He gave a history of uncomplicated typhoid fever ten years previously, occasional sore throats, sinusitis three years ago, and hay fever for the past seven years. He had had a tonsillectomy performed 14 years previously, and a tonsil and adenoid removal two or three years before, as well as removal of a turbinate from the nose.

Physical Examination—A diffuse, firm, rounded mass, about 5 cm. in diameter, was palpable in the right supraclavicular region, which was slightly elastic, slightly

fluctuant and only slightly tender. It was movable, but not freely so. The right suboccipital lymph nodes were also slightly enlarged, but not tender. There was a normal blood count, and roentgenograms of the chest and right shoulder were negative. The blood Wassermann was negative.

It was impossible to arrive at a definite diagnosis, the question of neoplasm, Hodgkin's disease and tuberculous lymphadenitis of the cervical nodes were considered.

Operation—November 24, 1937. An obliquely transverse incision was made corresponding to a crease in the neck, about 2 or 3 cm above the clavicle and deepened through the platysma and subjacent fat and descending cutaneous branches of the cervical plexus. After reaching the tumor, it was removed by alternately sharp and blunt dissection. The vessels were ligated with fine catgut and the wound closed with fine catgut for the platysma and interrupted fine silk for the skin.

Operative Pathology—The tumor was soft, but did not fluctuate. It was very vascular and had the appearance of a purplish plum on the surface, and, indeed, also on cut section. It was circumscribed, although here and there moderately adherent by fine fibrous adhesions to the surrounding structures. It lay quite deep in this region, the lower part of it lying beneath the middle of the clavicle. It was not attached to any large vein. During its removal a segment of it was cut out for frozen section. Doctor Stout reported that he felt convinced it was not tuberculosis, lymphosarcoma, or thyroid tissue. He could not tell what it was. A small lymph node attached to the tumor was removed with it. There were no other lymph nodes or masses encountered, and it was impossible to tell whether this mass was single or made up of two or three conglomerate nodes. It measured about 5.4 cm after removal, and had a smooth surface, though grossly nodular.

Pathologic Examination—Microscopic. Sections show that the tumor is made up of innumerable, small vascular spaces, most of which contain red blood cells. They are lined by large, swollen endothelial cells which in many areas reach a size of four or five times their normal dimensions. These cells are heaped up and sometimes almost fill the lumina. They also appear in places to have proliferated outside the lumina. A considerable search indicates that mitotic division must be very rare, since mitoses are not found oftener than one in 25 high power fields. At its periphery, the growth seems to be confined by a capsule. This is penetrated by blood vessels at intervals, but these vessels are lined by normal appearing endothelial cells. Accompanying the tumor and attached to one end is a lymph node which has dilated sinuses filled with red blood cells. At one point in the marginal sinus is a group of tumor vessels. This is at the end opposite the attachment of the tumor and must represent an invasion, or, more probably, a metastasis. This seemed to the pathologist to be a definitely malignant vascular tumor, the active elements of which are the endothelial cells. The question of terminology is a difficult one because of the great variety of names used for the malignant vascular tumors and the lack of accepted criteria for them. According to our classification, in this laboratory, this would be called a hemangio-endothelioma, because it is a vascular tumor in which the important malignant cells are atypical endothelial cells. *Pathologic Diagnosis*. Hemangio-endothelioma of supraclavicular region with metastasis to a supraclavicular lymph node.

The patient made an uneventful recovery, but in view of the diagnosis and the possibility of malignancy, it was advised that a lower neck dissection be performed. Accordingly, on December 27, 1937, about one month after the first operation, a lower right, radical neck dissection, according to the technic of Dr. George H. Semken, was performed.

Pathologic Examination—Microscopic. Sections of two of the lymph nodes removed show that there is a rather widespread fine fibrosis with lymphoid hyperplasia and dilatation of the lymph sinuses, but no evidence of the angiomatous growth. Sections taken from different parts of the cicatrix show that there is an unusual amount of scar tissue,

which encloses many groups of foreign body giant cells, which have apparently phagocytosed fragments of catgut, and are surrounded by an adult granulation tissue infiltrated with many lymphocytes and other inflammatory cells. Here, also, there is no evidence of tumor. *Pathologic Diagnosis* Cicatrix of supraclavicular region and chronic supraclavicular lymphadenitis.

Subsequent Course—The patient made an uneventful recovery from the second operation, and when seen six weeks later, the wounds had healed, a slight degree of trapezius paralysis was noted. Three months after operation, after the patient had been working for three weeks, he felt fairly well but complained of not gaining weight and of slight tenderness and numbness below the clavicle. At this time the scars were red but smooth, and the cosmetic result, excellent. The right trapezius is not paralyzed and there is no sign of neoplasm or enlarged lymph nodes.

Local, regional or distant metastases may, however, appear in this patient, so that frequent follow-up visits, with thorough physical examination, are advisable.

Dr. Arthur Purdy Stout, after a study of the subject, both from his own material and from the literature, has classified malignant tumors of the vascular structures of the extremities. This classification is applicable largely to other anatomic parts. The list is composed of the following tumors: Hemangiosarcoma, angiomyosarcoma, angio-endothelioma, malignant angioma, proliferative angiomatosis and malignant tumors of blood vessel walls.

The case herein reported appears to fall into the class of (angio) hemangio-endothelioma, presenting lawless growth of endothelial cells and involvement of a lymph node by metastasis from the tumor.

DISCUSSION—DR. GEORGE T. PACK (New York). The location of an hemangio-endothelioma in the neck, as illustrated in the case cited by Doctor Hanford, is quite unusual in our experience. These rare tumors seem to occur more frequently in the lower extremities, especially in individuals who have varicosities. Doctor Ewing considers venous stasis a possible etiologic factor. Such venous stasis may lead to endothelial overgrowth, sometimes benign and papillary, within the lumen and in other instances to solid endotheliomata, capable of metastasizing to lymph nodes and viscera.

CAVERNOUS HEMANGIOMA OF A CERVICAL NERVE

Case Report—A married woman, age 37, presented herself at the Vanderbilt Clinic in July, 1934, complaining of a lump in the neck of one year's duration, which was gradually increasing in size. There had been no inflammation, tenderness or pain. Except for general lassitude and frontal headache over a period of ten years, she gave a negative history. Her mother died of cancer and a sister of tuberculosis. She had had two normal pregnancies.

Physical Examination—A poorly defined mass, approximately 3 cm in size, was found deeply placed in the left lower cervical region. The question of lipoma, sarcoma, and cervical lymphadenitis were considered. *Laboratory Data* Urine negative. Wassermann negative. Hemoglobin 90 per cent. White blood cells 6,000. Red blood cells 4,500,000. Polymorphonuclears 50 per cent, lymphocytes 42 per cent, basophiles 2 per cent, eosinophiles 6 per cent. Roentgenologic examination of the chest revealed some old tuberculosis in the right upper lung. *Tentative Diagnosis* Lipoma.

Operation—An ill-defined mass, about 2 by 3 cm, was exposed in the posterior

triangle of the left side of the neck just above the clavicle. It proved to be a soft vascular tumor in intimate contact with one of the cervical nerves, probably the fifth. No enlarged lymph nodes were encountered. The tumor was found lying just beneath one of the deep muscles, which was split longitudinally in order to reach it. When well isolated, a fairly good-sized nerve was discovered leading into it and away from it. Because of the fact that this nerve was probably an important component of the brachial plexus (apparently the fifth cervical nerve), it was thought unwise to attempt to remove the tumor for fear of damaging the nerve and causing a paralysis of the arm. The tumor was accordingly incised and a small portion of its interior removed for biopsy. The capsule of the tumor was then closed and the muscles sewed together over it, the skin was then closed with interrupted silk sutures after a small goiter tube drain had been placed in the recesses of the cavity.

Pathologic Examination—Microscopic. Dr. A. P. Stout. Microscopic section revealed a large number of branching blood channels, many of which have thick walls. These walls are mainly fibrous, though smooth muscle fibers are irregularly encountered in them. There is some recent hemorrhage. The remaining tissue is dense fibrous connective tissue with few cells and no evidence of inflammation. The collagenous strands are jammed together. No nerves or nerve sheaths can be made out in this section. With Laidlaw's silver stain the cells are silver negative and very few fine reticulin strands are present. These are wrapped around the cell-containing spaces. Large pinkish, close-packed fibrous strands are predominant throughout the tissue. *Pathologic Diagnosis.* Venous racemose aneurysm (?) of the fifth cervical nerve.

Pathologist's Discussion.—"We are somewhat at a loss to interpret these findings. Apparently the lesion is essentially a vascular one and the vessels concerned in it are of the nature of veins or venous spaces which probably communicate one with the other. They are all atypical in appearance and are bound together with dense fibrous tissue so that they do not have definite, recognizable walls. I do not believe that it is a simple telangiectasis because of this bizarre appearance. I believe that the lesion is entirely benign."

Final Diagnosis. Venous cavernous hemangioma.

Subsequent Course.—The patient made an uneventful recovery, and when seen three months later still had a lump in the neck, but no symptoms otherwise. It was thought that the tumor might respond to some kind of radiotherapy. The patient has been seen occasionally since. She seems to have had no further neck trouble, her chief complaints being continuation of the frontal headaches, general malaise and coldness in the extremities. A basal metabolic study made in December, 1935, gave a -10 rate. Menopause symptoms may explain the picture.

In March, 1938, a small nodular tumor, about 2 cm. in diameter, was discovered in the right breast. Although believed to be benign, it was recommended that the tumor be removed as soon as possible and a section taken to determine its pathology. This will be undertaken shortly. The mass in the neck remains apparently unchanged.

Few cases of hemangioma of nerve trunks have been reported. In 1935,¹ only eight cases had been found. Five of these were definitely cavernous hemangiomas and possibly two of the others, the descriptions being inadequate for classification.

An apparently simple hemangioma may become locally invasive and destructive and even may metastasize to distant points.

REFERENCE

- ¹ Purcell, F. H., and Gurdjian, E. S. Hemangiomas of Peripheral Nerves, with Report of a Case of Cavernous Hemangioma of the Sciatic Nerve. *Am Jour Surg*, 30, 541, 1935.

DISCUSSION—DR GEORGE T PACK (New York) said that in Doctor Hanford's patient, the presence of an hemangioma in the fifth cervical nerve may not be a coincidental inclusion. The relationship of benign and malignant vascular tumors to the central and peripheral nervous system is curiously varied and interesting. Congenital hemangiomas have been seen which have the identical somatic distribution of certain spinal cord segments. He had recently excised a small, exquisitely sensitive nodule from the center of a large congenital cavernous hemangioma of the arm and hand, the nodule was found on microscopic examination to be a diffuse or unencapsulated, benign neuroma. Lymphangiomatous and hemangiomatous tumors are not infrequently coexistent with true von Recklinghausen's neurofibromatosis, and may constitute part of the cutaneous stigmata of this disease. A more specific regional relationship is illustrated in the peculiar von Hippel-Lindau's disease, an eponym for angiomas of the retina and cerebellum. The histologic relationship is demonstrated in the case of two rare, but well known tumors of the skin and subcutaneous tissues. The tumor of the glomus is a small bluish nodule occurring usually on the hands or feet, sometimes in the nail bed. It causes disability because of the extreme degree of pain which is constantly associated with it. The glomus is a congeries of arterioles which expands and contracts, and may have a function of regulating the flow of blood to the extremities. The glomus has an abundant sympathetic nerve supply as do other end-organs, the pain caused by the tumor is probably carried over afferent sympathetic fibers. Another tumor which is thought to originate from the neurocirculatory annex is the multiple hemorrhagic sarcoma of Kaposi. These tumors, which are often quite tender, vary greatly in their histologic make-up, so that different nodules on the same patient may show such different structures as angioma, neurofibroma, angiosarcoma, endothelioma, fibrosarcoma, etc., all variants of the tissues involved at the site of origin.

CHYLOUS ASCITES

REPORT OF THREE CASES

EDWIN P BUCHANAN, M D

PITTSBURGH, PA

THE OCCURRENCE of chylous fluid in any of the body cavities is a striking phenomenon. There are two main causes for the leakage of chyle from the thoracic duct. First, trauma producing a rupture of the duct, and second, diseased lymph nodes pressing upon the duct, with resulting extravasation of chyle into the peritoneal or pleural cavities. An occasional case has been reported from thrombosis of the left subclavian vein, from syphilis, nephritis, cirrhosis of the liver and heart disease.

In 1935, Lille and Fox¹ could find only 46 cases of traumatic chylothorax in the literature, including one case of their own which recovered after daily aspirations averaging almost two liters, over a period of four weeks, during which time the patient was put on a strictly fat-free diet, with almost immediate cure.

In 1910, Wallis and Scholberg² made a very extensive study of chylous ascites from the biochemical standpoint, and collected all of the published cases. The first record of milky ascitic fluid occurring in a diseased state was recorded about 250 years ago. "Previous to 1850, there were recorded 25 cases of milky peritoneal effusions," and in the 60 years following, Wallis and Scholberg were able to trace 173 cases, including three of their own. In the 27 subsequent years, from two to five articles appeared in the literature on this subject each year.

There is much confusion in the literature regarding the classification and differentiation of milky effusions. The two types usually mentioned are chylous and pseudochylous. In the opinion of the writer the majority of these cases, whether chylous or pseudochylous, are due to a greater or lesser degree of obstruction of the thoracic duct or its radicals. True, the chemical analysis of the fluids varies greatly.

Blankenhorn³ concludes that the term pseudochylous is misleading and should be discarded. In his study of five cases of pseudochylous ascites, he has shown definitely that the milky color of the fluid is due to emulsified fat in very finely suspended particles. Experimentally, by removing the cream from dogs' chyle and then extracting a large part of the protein, he was able to produce the so-called "pseudochylous" fluid. His work confirms that of Giardin.

Of the three cases herewith reported, one was on Dr. J. W. Robinson's service and the other two were personal cases. However, it was my privilege to treat Doctor Robinson's case during his absence and to perform one of the aspirations. I am indebted to him for permission to report it.

CASE REPORTS

Case 1—Service of Dr. E. W. zur Horst, R. W., female, age 46, was admitted to Mercy Hospital, Pittsburgh, February 24, 1930, complaining of abdominal distress and fullness of four months' duration. Her past history was essentially negative except for an hysterectomy, presumably for fibroids, at age 32.

Physical Examination—The abdomen was markedly distended, flat to percussion, and exhibited a fluid wave. A median operative scar extended from the symphysis pubis almost to the ensiform. Some edema of the ankles. Chest negative. Pulse, 76. Blood-pressure, 90/50.

Operation—Under local anesthesia, an incision about one inch in length was made, and 16 liters of milky fluid removed by aspiration. Upon standing, this had the appearance of a mixture of 75 per cent milk and 25 per cent coffee. After aspiration, a mass of considerable size could be felt in the epigastrium and left hypochondrium. It was quite tender, moderately fixed and seemed to involve the stomach. A barium meal given three days later showed the mass to lie above and behind the stomach.

Bacteriologic and chemical analyses of the aspirated fluid showed no growth on culture. Specific gravity, 1.025. Positive reaction for fat with Sudan III. Fat content, 0.8 per cent.

On June 23, 1930, 13 liters of chylous fluid were again aspirated from the abdomen.

On September 15, 1931, the patient complained of dyspnea and abdominal fullness. Roentgenologic examination showed a left pleural effusion with displacement of the heart to the right. Four liters of chylous fluid were aspirated from the abdomen and a similar amount of straw-colored fluid removed from the left chest.

On March 6, 1933, five liters of chylous fluid were withdrawn from the abdomen. No evidence of pleural effusion was noted, there was apparently a slight pleural thickening.

On April 19, 1935, the patient was readmitted to the hospital, complaining of pain in the left scapular region and lower back of two days' duration. Temperature, 102° F, white blood cells, 13,700, polymorphonuclear leukocytes, 83 per cent, mononuclear leukocytes, 12 per cent, lymphocytes, 5 per cent. Blood pressure, 108/72. Weight maintained at 190 pounds. A mass was present in the left hypochondrium, the size of an orange. No ascites was demonstrable. Dulness to flatness obtained over the lower third of the left chest.

On April 23, 1935, 750 cc of heavy chocolate colored fluid were aspirated from the left chest. *Pathologic Diagnosis* Massive hemorrhagic pleuritis with effusion. Secondary carcinoma of pleura (?) (The second diagnosis was predicated upon the finding of a few clumps of cells that were suggestive of columnar cell types.)

The patient was discharged, much relieved, April 30, 1935, but was readmitted July 14, 1937, complaining of pain in the upper abdomen of two days' duration. This was sharp in character and not related to meals. Attacks lasted one and one-half to two hours. She had lost 20 pounds during the last two years, and suffered from dyspnea and palpitation on exertion.

Operation—July 16, 1937. Under local anesthesia, a short incision was made in the left upper quadrant, through which a large mass was disclosed, situated below the stomach along its greater curvature. There were numerous nodules 1 to 2 cm in diameter on the parietal peritoneum. The abdomen contained about three liters of chylous fluid. A biopsy specimen was taken for histologic examination, the fluid aspirated and the wound closed.

Pathologic Examination showed the presence of an undifferentiated tumor cell, from which it was impossible to infer the location of the primary lesion. *Diagnosis* Abdominal carcinomatosis.

Analysis of the chylous fluid showed N P N, 267 mg, uric acid, 59 mg, creatinin, 14 mg, and cholesterol, 118 mg per 100 cc, sp gr, 1.018, coagulation, positive with heat and acetic acid, Rivalta test, positive, red blood cells and white blood cells present.

The patient was discharged July 24, 1937, and died September 8, 1937. No autopsy was obtained.

Case 2—Courtesy of Dr J W Robinson. E M, female, age 54, was aspirated by me August 30, 1930. Ten liters of yellowish chylous fluid were withdrawn from the abdomen through a short incision. Previously, a biopsy of axillary and femoral lymph nodes showed lymphoblastoma (Hodgkin's disease), and three weeks before I operated, eight liters of chylous fluid had been aspirated by Doctor Robinson. In all, four aspirations were performed, each of eight to ten liters, at intervals of three weeks. On October 10, 1930, she was discharged, and is thought to have died within a few weeks.

Case 3—Service of Dr George Kastlin. O S, colored, female, age 36, was admitted to Mercy Hospital June 24, 1934, with a history of having presented herself, seven weeks previously, at the Pittsburgh Skin and Cancer Foundation, complaining of abdominal distress, fulness and enlarged nodes on both sides of the neck. Because of a strongly positive Wassermann reaction, she was given 11 intravenous injections of neoarsphenamine. Treatment was discontinued because the abdomen was constantly enlarging, and there was a rapid decline in her general condition.

On July 24, 1934, eight days before admission, I performed a biopsy on the cervical lymph nodes which showed caseous tuberculosis. For 13 days following admission, up until the time of operation, the temperature rose to 102° F each day, occasionally to 103° F, pulse, 120. Roentgenologic examination of the chest showed no

definite evidence of tuberculosis. Blood counts were practically negative except for a mild secondary anemia. Wassermann, Lipoid negative, cholesterol four plus, Kahn four plus. The abdomen was markedly distended and evidenced the presence of fluid. There was a palpable mass of considerable size to the left of the umbilicus. *Preoperative Diagnosis*: Tuberculous peritonitis.

Operation—August 6, 1934. On opening the abdomen, about four liters of chylous fluid escaped. There was an enormous mass of retroperitoneal lymph nodes extending from the diaphragm to a point below the level of the umbilicus. The intestines were free and the lacteals engorged. There were adhesions about the spleen, which was very nodular. There were small pinhead nodules over the surface of the liver, resembling miliary tubercles. A large dermoid cyst of the ovary was removed, also a tubercle from the liver and a very small specimen from the retroperitoneal mass. There was a little capillary oozing which could not be controlled by adrenalin applied locally. Unfortunately the bleeding and coagulation time had not been determined preoperatively, but there was no jaundice or other reason to suspect a blood dyscrasia.

Following operation, there was enough bleeding from the wound to saturate the dressing. The wound edges were separated but no bleeding point could be found. Packing with thromboplastin and adrenalin was of no avail. Death occurred 38 hours after operation, apparently due to hemorrhage in a debilitated subject.

Autopsy—On opening the abdomen, it was found to contain a moderate amount of bloody serum and clots. The laboratory diagnosis was "early and late conglomerate and caseous tuberculosis of the lungs, liver, spleen, kidneys, fallopian tubes, and of the thoracic, cervical, mesenteric and retroperitoneal lymph nodes."

After removing the thoracic aorta, the thoracic duct was located. Small tuberculosis nodes were seen pressing upon it throughout its course and producing obstruction to methylene blue, which had been injected.

These three cases of chylous ascites are of interest in that the primary diagnosis in each was different—(1) carcinoma, (2) Hodgkin's disease, and (3) tuberculosis. The case with carcinoma was the only one that survived any length of time. It is rather remarkable that she should have lived almost eight years after the first appearance of ascites, and required only five tapings at increasing intervals—4, 15, 18 and 52 months. After the first two aspirations, when the amounts recovered were 16 and 13 liters, they never exceeded five liters and were as low as three. During the entire period she was kept fairly comfortable until within a few weeks of her death.

CONCLUSIONS

Repeated aspirations would appear to be the logical treatment of such a condition, when the primary diagnosis is an incurable disease. In 1912, Morse⁴ reported a case cured by venoperitoneal anastomosis. Such an operation should not be performed unless there is rapid reaccumulation of chyle after frequent aspirations, and then only when the primary condition producing the obstruction is a curable one.

REFERENCES

- ¹ Lille and Fox. *ANNALS OF SURGERY*, 101, 1367, June, 1935.
- ² Wallis and Scholberg. *Quart J Med*, Oxford, 3, 301, 1909-1910, 4, 153, 1910-1911.
- ³ Blankenhorn, M. A. *Arch Int Med*, 32, 129-139, July, 1923.
- ⁴ Morse, G. W. *Boston Med and Surg J*, 166, 294, 1912.

TRAUMATIC MYOSITIS OSSIFICANS

REPORT OF A CASE FOLLOWING FRACTURE AT THE ELBOW

SAMUEL KLEINBERG, M D

NEW YORK, N Y

A GENERATION ago it was the custom in the case of a fracture to immobilize the injured limb for many weeks, even many months, to assure bony union, leaving it more or less to chance to obtain satisfactory function in the adjacent joints. The result of this practice was that in many regions, notably the wrist, shoulder and knee joints, the ultimate range of mobility was greatly restricted, and hence the usefulness of the limb was seriously compromised. Gradually there came about an appreciation that through minimal, though always adequate, immobilization and concurrent or early voluntary motion in the adjoining joint or joints, a greatly improved functional result can be obtained. During the World War, many fractures in both the upper and lower limbs were splinted by braces or pin-traction, which permitted motion in the joints. Early motion in the treatment of fractures became almost a fetish. It is, of course, a fact that under certain circumstances mobilization of a joint near a fracture may be instituted very early. For instance, in an uncomplicated Colles' fracture that is well reduced, motion in the wrist and fingers may be begun within a week of the reduction. This is particularly important in elderly individuals in whom fibrous ankylosis of the wrist and finger joints is likely to occur. Similarly in the treatment of a well reduced and thoroughly immobilized fracture at the shoulder, motion may be instituted during the second or third week.

Sn Robert Jones demonstrated that in the treatment of fractures at the elbow in children, the fragments of the lower end of the humerus can, after reduction, frequently be effectively immobilized by acute flexion of the elbow. The attitude of acute flexion has the further advantage of limiting the amount of blood extravasation in the antecubital fossa. The original dressing is left on for ten days, after which it is removed daily, gentle massage is applied, the patient is encouraged to move the elbow through whatever range is painless, and the limb is again bandaged in acute flexion. The voluntary, painless motion is gradually increased, and may become normal or nearly so at the end of six weeks.

Early motion at the elbow, or at any other joint, is contingent on the absence of complicating factors. Furthermore, early motion in a joint adjoining a recent fracture is always to be voluntary and painless and never a passive, forced or painful act. Passive manipulation of a joint is permissible only when the fracture is healed, that is, in the late stages, when there is reason to believe that there are adhesions, intra- or peri-articular, which restrict mobility. And even in the late stages the manipulation must never

be forcible or rough, in order to avoid a severe reaction, with hemorrhage and the formation of new adhesions

The case herewith reported exemplifies the potential harm of over-enthusiastic or, more accurately, ill advised manipulation of a fractured elbow in the desire to obtain a satisfactory range of motion in a patient in whom there was an inherent tendency to ossification of the torn brachialis anticus muscle. Traumatic myositis ossificans is not common, probably few observers see more than three or four cases during an extensive surgical experience. Yet it occurs often enough, and has been described sufficiently thoroughly for us to have been acquainted with its clinical manifestations and therapeutic requirements. Traumatic myositis ossificans may occur anywhere in the body where there is a tear of a muscle or a ligament. An instance was recently observed by the writer, which occurred in the quadriceps muscle following repeated injuries in playing soccer. It is, however, most frequently found in the elbow joint following a fracture. It is difficult to explain why it occurs at the elbow more often than elsewhere, for the degree of injury is, as often as not, more extensive in fractures at other joints. Moreover, myositis ossificans occurs in only a very small per cent of the injuries in or near the elbow joint. One must, therefore, assume the existence in the particular patient of a personal idiosyncrasy, the biochemic nature of which is not understood. While, however, the pathogenesis of traumatic myositis ossificans is not yet comprehended, its treatment is well known. When once its presence is suspected and proven roentgenologically, the limb must be immediately protected from further injury or irritation. It may be sufficient, as it was in the case of traumatic myositis ossificans of the quadriceps muscle above referred to, to keep the patient in bed, interdicting all but the slightest motion in the adjacent joints, or it may be best, as in the elbow, to immobilize the limb in a rigid splint. The rest afforded by the immobilization favors the absorption of all or most of the calcific deposit, the resorption of the extravasated blood, healing of the torn muscular and ligamentous tissues, a rapid reduction of the swelling, and a return of the mobility of the elbow, except that degree resulting from the mechanical block of that portion of the calcified tissue which has become ossified. The earlier the lesion of traumatic myositis ossificans is protected, the more thoroughly and the more rapidly will the pathologic process subside. Serial roentgenograms of the lesion will show the gradual but continuous disappearance of the shadow of the calcified tissue, leaving only a spur or spicule of bone or perhaps no trace of its occurrence. Naughton Dunn,¹ in commenting on this complication of supracondylar fractures of the elbow, states "Passive movements, always contraindicated in injuries to the elbow, will increase the formation of new bone. The essential treatment is to continue rest of the joint in the position of flexion until the bony deposit has reabsorbed or has completed its ossification."

Case Report—R. G., female, age 5, was examined in October, 1936. Three months previously, July 17, 1936, she had sustained a fracture of the external condyle of the left elbow (Fig. 1). The limb was immediately immobilized in acute flexion and after

ten days, passive motion was begun. The elbow remained greatly swollen and sensitive. The child complained of severe pain and refused to move the elbow. The family became greatly alarmed about the stiffness of the elbow joint and, fearing that the child would grow up with a stiff and useless elbow, instituted daily forcible passive movements of the elbow. During this manipulation the child screamed and begged to be left alone. The manipulation was continued persistently and ardently. The child continued to scream and became fearful of the approach or proximity of her mother or uncle who did the stretching. The child was adjudged to be nervous and not to be minded. When first seen by the writer, the child was frightfully apprehensive. The left elbow was greatly



FIG 1—July 17, 1936 Oblique fracture of the external condyle of the left humerus. There is downward and forward displacement of the condylar fragment.

swollen and very sensitive. There was marked tenderness to pressure in the antecubital fossa and very little motion in the elbow joint. The diagnosis was readily established and rest of the elbow in a flannel sling was advised.

The patient was next seen one month later, and was not improved. The elbow was still markedly swollen and sensitive. Roentgenologic examination showed healing of the supracondylar fracture (Fig 2 A), but, in addition, an extensive calcific deposit in the antecubital fossa in the line of the brachialis anticus muscle and the anterior surface of the capsule of the joint, extending from the shaft of the humerus, two inches above the joint line, down to the coronoid process of the ulna (Fig 2 B). A lateral view showed that the tear of the soft tissues involved, as it so often does, a very wide area beyond the fracture line. As happens in so many other fractures, the break in the continuity of the external condyle was a simple one, and, by far, not the most important element in the injury. Further inquiry revealed that the elbow had really not been rested. The child had been urged to move it and, in fact, manipulation, although less vigorous than previously, had been continued, the mother having an obsession about a permanently stiff elbow resulting.

The entire arm was, therefore, immobilized in a plaster of paris bandage. Three

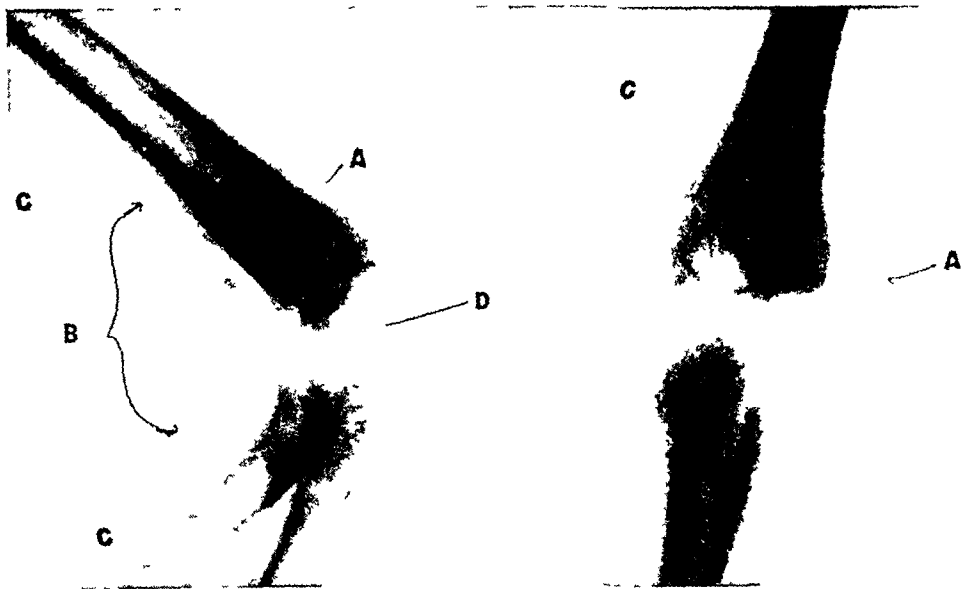


FIG 2—November 10 1936 Four months after fracture Note at (A) considerable bone formation along the posterior and lateral surfaces of the humerus (B) Marked calcareous deposit along brachialis anticus muscle There is marked swelling of the soft tissue (C) The capitellum (D) is displaced downward and forward

FIG 3

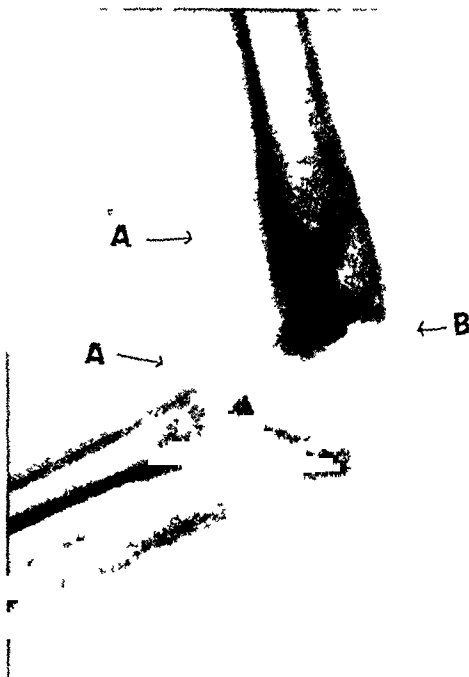


FIG 4

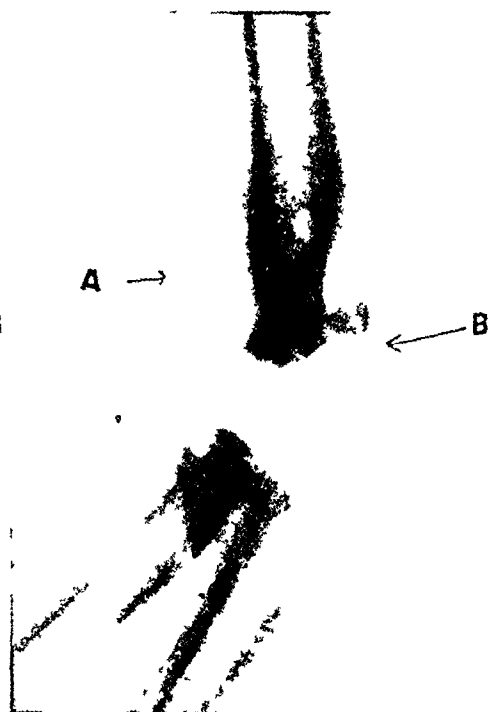


FIG 3—November 30, 1936 (after 20 days of plaster immobilization) Compare with Figure 2 and note the marked reduction in the swelling of the peri articular soft tissues and in the amount of calcareous deposit (A) There is a beginning spur formation (B) on the posterior surface of the humerus

FIG 4—February 25, 1937 (three and one half months after secondary immobilization was instituted) Note the complete disappearance of the calcareous material from the antecubital fossa except for spur formation (A) on metaphysis of humerus There is a posterior spur (B) which is likely to permanently, though only slightly, limit extension of the elbow

weeks later the elbow was found to be of almost normal size and only slightly sensitive. There was 10° of voluntary painless motion. A roentgenogram (Fig 3) showed a marked reduction in the soft tissue swelling and in the extent of the calcareous deposit. The elbow was again immobilized for three weeks, during which time the sensitiveness disappeared and the range of motion increased. No treatment of any kind was applied thereafter. The child, whose confidence had by this time been won, was encouraged to use the arm and move the elbow through as great a range as was possible without causing pain. By March 1, 1937, there was a voluntary range of 75° of motion, from 90° of flexion to 165° of extension, and complete pronation and supination. A lateral roentgenogram (Fig 4) showed a spur formation at (A) on the anterior surface of the metaphysis of the humerus at the upper limit of the calcareous deposit, and complete absorption of the rest of the deposit. A bony spur was also seen on the posterior surface of the humerus (B) on the proximal side of the epiphyseal line. The anterior and posterior spurs undoubtedly accounted for the restriction in motion. But the patient already had 75° of motion in the elbow, which is a useful range even if there were to be no further increase of motion. As a matter of experience the mobility of the elbow is very likely to increase. And in any event, at a later time, if desired, either or both bony spurs might be removed by operation.

SUMMARY

A case of traumatic myositis ossificans is reported, which occurred in a child following a fracture at the elbow. The fracture was accompanied by extensive soft tissue damage, particularly in the antecubital fossa where there occurred a thick calcareous deposit along the attachment of the brachialis anticus muscle. The efforts to obtain motion in the elbow by forcible passive movement served to perpetuate and perhaps to increase the swelling, as the enlargement of the elbow three months after the fracture was reported to be nearly as great as that noted directly after the injury. Complete rest of the elbow by immobilization of the limb in a plaster of paris bandage caused a recession of the swelling, resorption of most of the calcareous material and the return of a satisfactory range of motion in the elbow. We must, therefore, bear in mind that if, following a fracture at or near a joint, especially the elbow in children, there is persistent pain, swelling, sensitiveness and stiffness of the joint, one must suspect the deposit of calcium salts in the injured soft tissues. If the existence of this lesion, a traumatic myositis ossificans, is confirmed roentgenologically, the most effective treatment is immobilization of the limb until all the swelling and sensitiveness disappears, irrespective of the duration of the symptoms or the time it takes for them to vanish.

REFERENCE

- ¹ Dunn, Naughton. Supracondylar Fracture of the Elbow. Brit Med J, 2, 663, October 3, 1936.

MEMOIRS

FRANCIS REDER

1864-1936

MAY 8, 1936, marked the passing of one of our most unique and lovable characters, Dr Francis Reder. A member of our association since 1911, he was elected a senior member in 1932. Faithful in attendance and participation for many years, his genial presence will be greatly missed.



FRANCIS REDER, M.D.

Francis Reder was born at New Athens, Illinois, January 6, 1864. His father, Dr Franz Reder, a graduate of Heidelberg University, migrated from Germany in 1848, and Francis Reder was graduated in turn from Smith Academy and St. Louis Medical College now Washington University Medical School, in 1884. After intern services at St. Louis City and Female Hospitals, he spent over two years with Dr G. A. Gerster at the German Hospital in New York City, and from 1888 to 1891 in European universities and clinics.

In 1897, after several years of private practice, Doctor Reder specialized in general surgery. He was a member of the St. Louis Medical Society, which he served as President in 1932, and of the Missouri State and American Medical Associations, St. Louis Surgical Society, Southern Surgical, Southern Medical, American Association of Gynecologists and Obstetricians, and the American College of Surgeons. On November 13, 1935, he was elected an Honor Member of the St. Louis Medical Society. In 1910, he was an invited guest of the Twenty-third Congress of the Association Française de Chirurgie, in Paris.

In 1897, he married Ella Castle of Quincy, Illinois, and is survived by his widow and three children.

Honored at home and abroad, loved and respected by all who knew him, he possessed the admirable attributes of professional dignity, ability and congenial personality. To him the world was a stage, and his profession the plot, in which he labored daily, administering to the needs of his fellow men.

FRED W. BAILEY

JOHN ROBERTS CAULK

1881-1938

JOHN ROBERTS CAULK, our genial, forceful, deeply scientific, and much beloved fellow, passed away, October 13, 1938. He was born in McDanel, Maryland, October 30, 1881, of a family established in that state by one John Caulk, who came over from Scotland with a land grant from Lord Baltimore.

Attending, successively, several Maryland schools, he received his medical degree from Johns Hopkins University, in 1906, and after serving as Assistant Physician in the Union Protestant Infirmary at Baltimore, he became Assistant Resident Surgeon and the first Resident in Urology at Johns Hopkins Hospital. He came to St. Louis, in 1910, to make his home, accompanied by his wife, Mrs. Bessie Harrison Caulk, who survives him and was ever his unfailing helpmate.

In 1910, shortly after his arrival in St. Louis, Doctor Caulk was appointed Instructor of Genito-Urinary Surgery at Washington University Medical School, and served under successive titles, including that of Professor of Clinical Genito-Urinary Surgery, which he held until his death.

St. Louis has, for a century or more, profited to an unusual extent from the professional activities of outstanding medical men who chose this center for carrying on research, and the practice and teaching of medicine. One might hazard that among these, none came better founded in his special field than Doctor Caulk, none has proved more expeditious in solving the surgical problems that confronted him, and it is likely that few had been equally blessed with the combination of pleasing manner, stimulating personality and live consciousness of his opportunities of service to the profession and the public that was characteristic of Doctor Caulk throughout his all too short working period. Public recognition came early, but it affected neither his personal balance nor the intensity of his professional pursuits. He had surgical hobbies, not everywhere accepted, and he was not without personal critics, but mostly those who knew him least.

To undertake to enumerate his original contributions to the science and art of urology, or his writings, or to name the scientific societies that claimed him as a member would for want of space defeat its own ends, but this is a tribute of friendship, not an archive, and we will turn to his more personal side.

Doctor Caulk was possessed of a most charming personality and an air of refinement lent a delightful atmosphere to his presence. He was most entertaining and was blessed with a keen sense of wit and humor, though he could be serious minded, especially when a medical or surgical problem was under discussion. He was a very dynamic individual and was embodied with unusual energy for work. He was a great fellow to work at full speed and

play in the same manner. He was courteous and genial at all times and all his colleagues, especially those fortunate enough to have been closely associated with him, would sing his praises for his pleasant attitude at all times. He was most enthusiastic about his work and was constantly searching for new problems to solve. He was fortunate in having a multiplicity of qualifications for work and play which permitted him to do both without the sacrifice of either. His two chief hobbies were horseback riding and sailing. In the summer he loved the latter better than anything else and practically lived on his sailboat. In the spring and fall horseback riding was his most pleasant diversion. In the winter his books and extensive contributions to medical journals occupied his time at night, and the day found him laboring with unusual skill and enthusiasm on various urologic problems.

The true test of character comes through adversity even more than success. For more than a year, while in the full possession of all his mental faculties, he saw himself being eliminated from active work by a malady that proved beyond control. Toward the end he suffered almost continuously with uncontrollable pain, all of which he endured with a stoicism that any of us would envy. His personality will long be remembered by those with whom he came in contact, but the silent influence of his constructive touch in his chosen field will be active long after his personality is forgotten.

VILRAY P. BLAIR

JOHN HENRY NEFF, JR

1887-1938

DR JOHN HENRY NEFF, JR, a fellow of the Southern Surgical Association since 1926, and vice-president in 1934, was born, September 12, 1887, at Harrisonburg, Va, and died, November 8, 1938, at University, Va. He was



JOHN HENRY NEFF, JR, M D

the son of Dr John Henry Neff a practitioner in the city of his birthplace. After graduation from his local high school, he completed the classical course at the University of Virginia where he received the A B degree in 1907.

Three years later he was graduated from the same institution with the degree of M D. In 1916, he married Miss Harriet Louise Fitzgerald, of Houston, Tex., who survives him, together with two sons and a daughter.

Doctor Neff's professional life was unusual in two respects. He had perhaps the soundest background of general surgery upon which any urologist of his age has based his specialty. Seven years of house training in general surgery under Prof. Stephen H. Watts was followed by two years as Acting Associate Professor of Surgery in the University of Virginia School of Medicine. During this time he became a conspicuously competent general surgeon. In the latter portion of this period, he began to interest himself in urology and, in 1919, became Adjunct Professor, advancing through the grade of Associate Professor to that of Professor of Urology, the rank he held at the time of his death. The second unusual aspect of his career resides in the fact, reflecting his remarkable qualities of mind and character, that he was entirely a self-taught urologist. No course in urology and no trained urologic chief are responsible for his development. In spite of this lack, a possibly insurmountable handicap to lesser men, he so perfected himself as to be recognized for his professional attainments not only by a large clientele and by his local colleagues, but also by the best of his fellow urologists. Such recognition was expressed by his election to membership in the American Urological Association and in the American Association of Genito-Urinary Surgeons. Although not a prolific writer, he added from time to time sound and thoughtful contributions to the literature of his specialty. He evidenced on every occasion almost faultless surgical judgment, based upon a wide knowledge of pathology. As an operator, he was methodical, careful and thorough, respecting tissue profoundly, bold where boldness was justified. He learned transurethral prostatic resection at an age when a new and exacting technic is doubly difficult to master. His last professional paper, presented by an associate before the Virginia State Medical Association, a month before his death, dealt with his experience with this procedure and revealed how successful the new method had proven in his hands.

Doctor Neff was outstanding in the community for his kindness, his never-failing cheerfulness, his level-headedness and his courage. Patients reacted toward him with a devotion that was almost religious in its intensity, an emotion duplicated by students and house staff alike. Without exception, his university colleagues regarded him with profound affection. They looked to him for sound judgment in difficult university and medical school matters, particularly where the ethics of a situation might not be entirely clear. When he believed that a question of ethical conduct was involved, his decisions were rapid, inflexible and always in behalf of what he considered justice and honesty. Although unyielding in such decisions, a deft removal of the sting of an opposed opinion through a mellow tact and a striking modesty, prevented antagonizing the opponent. To his acquaintances he was always considerate, and to his intimates one of the most charming of companions.

Doctor Neff, during college days, was one of the outstanding backs of the South and later a coach of college football. He was an ardent fisherman, the streams of Canada, and the tidal waters of his native state as well as local pools and brooks were the scenes of his successful sportsmanship. He was a tennis player of at least local note. When outdoor sport was impossible he found his relaxation in card playing, at which he was no negligible opponent, and in the reading of books. His literary taste was at the same time catholic and eclectic. Although professional duties prevented church attendance, he kept in touch with the activities of his denomination and contributed generously to its support. On the night before his death, he was elected to the vestry of St. Paul's Episcopal Church. In addition to the memberships in professional societies already cited, he was a Fellow of the American College of Surgeons and a member of Phi Beta Kappa, Sigma Xi and Alpha Omega Alpha.

After contemplation of his unusual record and his fine qualities of personality, one cannot wonder that the University of Virginia and the world of urology felt the untimely death of Doctor Neff as an irreparable loss. A tower of strength to all who knew him had fallen, a light that used to illuminate and cheer had gone out. The Southern Surgical Association is richer for having accorded him fellowship.

EDWIN P. LEHMAN

ELLIS FISCHEL

1883-1938

ELLIS FISCHEL, a product of Harvard College, and Washington University Medical School, had interned at our City Hospital and pursued postgraduate studies in Berlin, Vienna, Munich, Beine, was 29, highly trained, rugged,



ELLIS FISCHEL, M D

timeless, ambitious when he and I entered upon a rather lengthy professional association

He served at some time on the staffs of ten St. Louis Hospitals, he also taught surgery at different periods in both of our local Universities, and became a member of almost every local and national society to which a surgeon is eligible

There seem to have been three distinct and separate currents discernible in his life's work. He was, first of all, a sound surgeon with a very large

operative experience, procedures of almost unbelievable magnitude planned to cope with the regional spread of cancer were with him a matter of almost daily, successful routine. The second phase of his career, which seems to deserve special attention, is that which concerned itself with the founding and growth of the St. Louis Clinics. He was Secretary or President of this organization during its first six years, then continued as the mainspring of its existence for all the subsequent years of his life. He thereby did more, it has been said, than anyone else in our community in contributing to coordinated and publicized *postgraduate medical teaching* in St. Louis Hospitals. The third and most notable consideration which engaged most of his professional life was connected in one way or another with the study and treatment of cancer; he became successively a member of the Board of Directors of the American Society for the Control of Cancer, Chairman of its St. Louis Committee, then Chairman of its Missouri State Committee. He had been, since 1919, a member or Secretary of the Barnard Free Skin and Cancer Hospital (of our city) medical staff when, in 1933, he became a member of that institution's Board of Directors as well. He was Chairman of the Committee on Cancer of the Missouri State Medical Association for the last seven years of his life, he headed our State Cancer Commission selected by the Governor to locate, plan and construct our State Cancer Hospital which has, since his passing, deservedly been named in his honor.

His accomplishments prove that he possessed a type of imagination which enabled him to glimpse what lay beyond our common horizon, his work with the St. Louis Clinics and on the cancer problem show him to have been an exceptionally gifted executive as well.

In many instances he displayed a type of courage which goes far toward making a man seem indomitable, as when, a Harvard Senior, he won the golden bat conferred each year for the highest batting average on that rare type of player who instinctively steps forward to meet the pitch instead of drawing back from the plate as do so many others. Just as on the campus, so later, too, life's major issues were always met by him without flinching. He may be said truly to have been a stoic also, because no one ever heard him complain of blows which would have prostrated a less well poised man.

A summary of all his endeavors points unerringly toward a life of service to mankind. His efforts in behalf of the St. Louis Clinics and of the cancer cause certainly were never directed toward his own personal advancement although material reward was, of course, inescapable for a man whose attainments were far in excess of the measure to which we are accustomed.

This cultured man, finished surgeon and surpassing organizer was only 54 when devotion to his chosen field of professional endeavor led directly to his untimely end, he was hastening to Governor Stark's office for a conference regarding final details of the State Cancer Hospital design when there was a highway crash, ruthless Fate had decreed that the dream of his mature years should not become a reality for himself.

WILLARD BARTLETT

BOOK REVIEW

MODERN SURGICAL TECHNIC By MAX THOREK, M D, K L H (France), K C (Italy) With a foreword by DONALD C BALFOUR, M B, M D (Tor), LL D, Complete in three volumes, with 2,147 illustrations Philadelphia, J B Lippincott Co, 1938

In spite of the fact that there are several very excellent works covering the field of General Surgery, these three volumes, devoted to modern surgical technic, furnish a wealth of information presented in a different manner than in most other text-books. For every conceivable surgical lesion there are one or more accepted surgical procedures described. These procedures have been carefully and wisely chosen so that only the best ones are included. The work is not padded with superfluous, antiquated or unusual operations which would have no value as a reference for the active surgeon. The general plan of three volumes is worthy of mention. Each volume is divided into two Parts. Each Part is preceded by a descriptive page entitled "Orientation." This gives, in brief, a general survey of the contents of the following Part. Part One consists of six chapters dealing with "The Surgeon and His Art, The Surgeon and His Patient, Postoperative Considerations, Operating Pavilions and the Operation in General, Sterilization of Surgical Instruments, and Anesthesia." These chapters constitute an introduction to the actual text which follows. A relatively large amount of space is devoted to sterilization, the arrangement and position of the operating team, the illumination of the operating rooms, the donning of gloves and gowns, descriptions of various anesthesia machines, and innumerable other details which we presume are necessary to make a work on surgical technic complete. Part Two concerns itself with the "Surgery of the Head and Neck," and a very excellent treatise on "Plastic Surgery." A good, standard operative procedure for thyroidectomy is completely described. The dangers and hazards associated with this operation are mentioned and the ever-present pitfalls are emphasized. It is noted that the only operative treatment of Ludwig's angina given, is drainage through the floor of the mouth. Nothing is said concerning a direct attack on the submaxillary nodes. This procedure has recently been reported as being very satisfactory in several cases of this distressing condition. The chapter ends with 42 pages devoted to the various types of skin grafting.

Volume Two deals with the surgery of nerves, blood vessels, bones, thorax, and breast. The more popular procedures used to-day in dealing with lesions of the nerves and blood vessels are graphically illustrated. A description of Cile's adrenal denervation for hypertension is presented. Nothing is said, however, of Cile's more recent work, namely, celiac ganglionectomy, which operation we believe has largely replaced the adrenal denervation for hypertensive cases.

Throughout the world, there is an ever increasing number of bone lesions and fractures, due to the increasing number of motor car accidents, and to

the tremendous increase in the use of industrial machinery of all sorts. This particular branch of surgery is quite properly attracting more and more attention. The so-called "Traumatic Surgeon," one who has preferably had previous general surgical training, is rapidly coming to the fore. Three hundred thirty-seven pages devoted to orthopedics, fractures, and dislocations provide a very complete guide to the proper management of these cases. The author is very conservative concerning open operations and believes that if properly handled many cases now subjected to open operation could as well be treated by closed methods.

The various standard procedures of handling breast lesions are presented. The author stresses the necessity of a radical block dissection of the nodes in the supraclavicular fossa, when these can be demonstrated to be involved. He has performed 72 such operations and was able to "cure a few cases formerly considered unoperable and abandoned to fate." The use of electro-surgery in radical mastectomy is felt to be the method of choice. Such a procedure is described in considerable detail.

The technic of pulmonary surgery is well presented. The reviewer was delighted to see that Claude Beck's work on the "Surgery of the Heart" was given proper recognition. A very complete, although concise, résumé of Beck's operations is given and very well illustrated in the closing pages of Volume Two.

The first part of the third volume concerns itself with the "Surgery of the Abdomen" and the second part with the "Pelvic Region," both male and female. Very excellent descriptions of all abdominal operations are given. The author has carefully chosen those procedures which, in his opinion, are most practical. We presume that the various operations for suspension of the stomach were inserted for historic interest and in order to make the work complete. These operations are seldom undertaken at the present time. The author favors the removal of the gallbladder by electrocoagulation and describes in detail his own operation for this condition. The subject of hernia is well presented. The newer methods of repair by fascia transplants, as well as the older methods are included in the discussion.

For resection of the rectosigmoid and rectum, the technic of Fred W. Rankin is described. The illustrations accompanying the text on this operation are by "the courtesy of Dr. Fred W. Rankin." The last 307 pages are devoted to gynecologic operations and surgery of the genito-urinary organs.

Apparently Doctor Thorek was trained in a school in which his teachers were general surgeons in the broadest sense of the word. These men were capable of removing an eye, draining a mastoid, or a brain abscess, operating upon any acute throat lesion, caring for elective orthopedic or emergent fracture cases, suturing a lacerated heart, performing any intra-abdominal surgery including gynecology and urology. Recently specialization has developed to such a degree that the so-called general surgeon is rapidly disappearing. However, there are a few left in the large metropolitan centers and a great many in the smaller cities and in the sparsely populated country districts throughout the land.

MERRILL N. FOOTE

PHILADELPHIA ACADEMY OF SURGERY

THE SAMUEL D GROSS PRIZE

FIFTEEN HUNDRED DOLLARS

ESSAYS WILL BE RECEIVED IN COMPETITION FOR THE PRIZE UNTIL JANUARY 1, 1940

THE conditions annexed by the testator are that the prize "shall be awarded every five years to the writer of the best original essay, not exceeding one hundred and fifty printed pages, octavo, in length, illustrative of some subject in Surgical Pathology or Surgical Practice founded upon original investigations, the candidates for the prize to be American citizens "

It is expressly stipulated that the competitor who receives the prize shall publish his essay in book form, and that he shall deposit one copy of the work in the Samuel D Gross Library of the Philadelphia Academy of Surgery, and that on the title page it shall be stated that to the essay was awarded the Samuel D Gross Prize of the Philadelphia Academy of Surgery

The essays, which must be written by a single author in the English language, should be sent to the "Trustees of the Samuel D Gross Prize of the Philadelphia Academy of Surgery, care of the College of Physicians, 19 S 22d St, Philadelphia," on or before January 1, 1940

Each essay must be typewritten, distinguished by a motto, and accompanied by a sealed envelope bearing the same motto, containing the name and address of the writer. No envelope will be opened except that which accompanies the successful essay

The Committee will return the unsuccessful essays if reclaimed by their respective writers, or their agents, within one year

The Committee reserves the right to make no award if the essays submitted are not considered worthy of the prize

EDWARD B HODGE, M D,
CHARLES F MITCHELL, M D,
CALVIN M SMYTH, JR, M D,

Trustees

Philadelphia, February 1, 1939

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M D
1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English

Exchanges and Books for Review should be sent to James T Pilcher, M D, Managing Editor, 121 Gates Avenue, Brooklyn, N Y

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa



PAPILLEDEMA WITHOUT INTRACRANIAL PRESSURE (OPTIC NEURITIS)

WALTER E DANDY, M D

BALTIMORE, MD

ALTHOUGH papilledema is the most significant objective finding in brain tumors it is by no means pathognomonic of this lesion. In 1937, the writer¹ reported a series of cases in which there was bilateral papilledema with intracranial pressure and yet no brain tumor. This condition, whatever the unknown cause or causes may be, could be safely differentiated from the tumor group by ventriculography. The ventricles were uniformly small, but showed no displacement. In the course of a most variable period of time, the intracranial pressure subsided and the patients remained permanently well. They were spared major operative procedures which would otherwise have been indicated, only a subtemporal decompression was necessary to preserve life and vision pending subsidence of the intracranial pressure.

The present report is concerned with another, even larger, group of cases having papilledema, usually bilateral, at times unilateral, frequently with hemorrhages in the eyegrounds, and usually with a mild degree of headache and with varying degrees of visual loss. This group differs from the foregoing one in the absence of intracranial pressure. The underlying pathologic process causing the papilledema, whatever its character or the underlying cause, is, therefore, largely of *local* origin and may be classified as "optic neuritis," "papillitis," or "retrobulbar neuritis," if it is understood that these designations do not connote an inflammatory process, which it may or may not be. There can be little doubt that the pathologic process is, in many instances at least, not strictly confined to the optic nerve or nerves because of the frequent coexistence of other signs and symptoms, such as headaches, diplopia, dizziness and perhaps nausea and vomiting. But the intracranial involvement beyond the optic nerves is rarely great or severe. There can also, I think, be no doubt that this is not strictly a pathologic or clinical entity, for in a few cases at least, the ophthalmologic picture is an initial manifestation of multiple sclerosis, and in one patient who died 14 months later the microscopic sections of the brain showed diffuse chronic encephalitis involving the cerebral cortex. However, the number of such cases, studied over such a long period of time, is so small that one can be

equally certain that multiple sclerosis or encephalitis is the exception rather than the rule. From the evidence at hand it is not possible to say that the pathologic process is one of demyelination in the optic nerves, or an inflammatory or perhaps some other process.

On the whole, the pathologic process and its signs and symptoms are acute or relatively so, it subsides spontaneously with or without a permanent visual defect and has almost no tendency to recur (a single exception). In most of these cases the differential diagnosis from a brain tumor has been made by ventriculography, and the absence of intracranial pressure has been determined by manometric readings of the spinal fluid by spinal puncture. In some of the later cases the clinical picture has seemed adequate to make the diagnosis without either ventriculography or spinal puncture. The principal differential diagnostic test of this condition is a rather precipitate loss of vision—much too rapid to be possible from the effects of intracranial pressure. One also considers, though with less assurance, the relatively slight headache accompanying such a high grade of papilledema with retinal hemorrhages.

Since there is no intracranial pressure, operations upon the brain are not indicated. It is cases of this kind that have been subjected to exploratory craniotomies with negative findings, to decompressions and to operations upon the paranasal sinuses. The latter operations have been performed on the assumption that an inflammatory process has extended through the bone of the skull and into the optic nerves. And many teeth have been pulled in the search for an inflammatory focus.

Since the pathologic process is one of relatively short duration and clears spontaneously, it is not surprising that excellent results have been claimed following any therapeutic efforts, whether surgical or medical, but the results are, of course, *post hoc, propter hoc*.

Forty-four cases of this condition are included in this report, and the end-results presented in 31. From the remaining 13, no answer has been received to inquiries by letter. The cases are spread over the past 15 years. The results of the study are presented in the accompanying table and are summarized in the ensuing résumé.

Sex and Age Incidence—Curiously enough, females are almost three times as frequently affected as are males—the exact number of each being 32 and 12. Such a great difference in the sexes must carry some significance but I know of no explanation.

This condition occurs in every decade of life up to the seventieth year, and with surprising regularity except in the second decade where the number was more than double. The actual numbers by decades were 6, 15, 6, 6, 7 and 4.

Résumé of Signs and Symptoms Duration—To the time of admission to the hospital, the condition has existed less than one month in 21, or nearly half of the cases, less than three months in 31, 70 per cent of the

cases It was less than six months in 38 cases, or 86 per cent, less than one year in the remaining six In one case, under observation almost from the beginning of the illness, the patient was practically blind within five days, three days later the visual fields and visual acuity were normal, and one year later the vision was still perfect There can be no doubt that many patients who appear months or years after an initial attack of visual loss have had edema at the onset, and at this late date there remains only some evidence of pallor in the optic disks

Headache—In 37 cases from the series, headache was a conspicuous symptom, in five it was absent, and in two not mentioned In most instances the headache appeared almost simultaneously with loss of vision It was never as severe as in brain tumors, although instances of the latter without headache are by no means uncommon At times the headache was bilateral, and at other times unilateral Often it was in the frontal region, or behind the eye, and not infrequently more of a stinging, boring pain rather than an ache

As noted above, the relatively slight degree of headache was in such marked contrast to the severe grade of papilledema that the diagnosis of an intracranial neoplasm was considered unlikely

Diplopia, Nausea, Vomiting, Dizziness and Convulsions—Double vision was present in 13 cases and absent in 25, *i e*, it was present in roughly one-third of the cases Only in three cases was there an extra-ocular palsy and in one of these it was bilateral One of the unilateral palsies was the case of encephalitis, the bilateral palsy was in a particularly severe illness with total blindness which has persisted though the patient is otherwise well, 11 years later, the third case has not responded to our letter of inquiry The appearance of diplopia means, of course, that the pathologic process has extended beyond the optic nerves Except in the cases where an extra-ocular palsy has followed, the diplopia has always been of short duration—in one instance only 30 minutes

In nine cases there was nausea, and in 12 vomiting, but in two of the latter it was said to have followed medicine by mouth In no instance was either the nausea or vomiting prolonged or severe, and in many vomiting occurred only once

Dizziness occurred in ten cases and was never severe

Convulsions were present in none This negative note is recorded because it is fairly important evidence against any degree of cerebral involvement

Other Signs and Symptoms—One patient had numbness of the face, she has since been followed (two and three-fourths years) and has had no return of it Another had weakness of the right arm, polydipsia and palsy of the right sixth nerve, her subsequent course is unknown, it may be a case of multiple sclerosis Another patient subsequently developed characteristic signs and symptoms of multiple sclerosis, *i e*, ataxia, Romberg, staggering gait and urinary incontinence A bilateral Babinski sign was elicited in one

patient, it has since disappeared and she remains perfectly well. Bilateral ataxia was noted in another patient, who probably had an acute encephalitis following pneumonia (*Streptococcus*), except for a severe loss of vision she recovered completely. Buzzing in one ear was noted by one patient whose subsequent course is not known, and by another who recovered with total blindness but with no return of the buzzing, bilateral exophthalmos of low grade developed during the present illness and subsequently disappeared.

In three patients adiposity was excessive. In two, the menses had disappeared, and in the third, they subsequently disappeared but returned following injections of hypophyseal extract. In each of the above three adipose individuals the increased weight had long antedated (one, three and 12 years) the visual disturbance and could, therefore, have had no bearing upon it. Since this abnormal grade of adiposity is so commonly associated with menstrual irregularity and loss, it is probable that this disturbed function was also not related to the papilledema. However, in one patient the amenorrhea developed only one month before her visual loss and she dated the present illness from it.

Polydipsia was a symptom in one case and was perhaps a manifestation of encephalitis.

Three patients in this series had hypertension—two of moderate (170, 168) and one of severe grade (220). The frequent association of papilledema with hypertension of severe grade is well known. I have excluded from this series those cases in which the papilledema appeared to be directly related to the hypertension. In the three cases included in this report, there can scarcely be a doubt that the hypertension was entirely independent and unrelated. One patient with a blood pressure of 178 died eight years later following an abdominal operation, the findings of which are unknown. Her vision had remained unchanged in the interim. The most surprising case was that of a colored woman, age 44, blood pressure 220/110. Following an acute visual disturbance, with 4 D of papilledema and hemorrhages in both eyegrounds, the patient's vision returned almost to normal and has remained so for six and one-half years, and despite continuous hard work she is symptomless and her blood pressure remains 220/110. Her blood pressure surely has nothing to do with her acute visual episode. The third patient, whose pressure was 180, cannot be traced.

In only a single patient was there a positive Wassermann reaction, this was positive both in the blood and spinal fluid. Whether or not it was related to the papilledema cannot be determined. The eyegrounds rapidly became normal during vigorous antisyphilitic treatment. The story is so similar to that of so many other cases—all without syphilis—that I doubt the relationship.

Etiology—That this series of cases contains not a single pathologic entity is shown by the fact that there is certainly one and probably a second case of multiple sclerosis, and one and perhaps two more cases of encephalitis.

The association of papilledema with both of these lesions is well known. But I do not believe any of the remaining cases could fall under either multiple sclerosis or encephalitis.

A nonspecific inflammatory origin is suggested in three cases. In one instance there was tenderness and swelling of one eyelid at the onset of symptoms, and the papilledema developed only in the corresponding eyeground which contained numerous small hemorrhages. Five and one-half years later the center of the disk was filled with a scar that entirely concealed the entering blood vessels, the visual acuity was 20/20 in each eye but a temporal defect remained in the affected eye. In another case, the left eyelid was swollen and painful and there was lacrimation at the time of onset of the visual change. The other eye had been blind from birth. She had had unilateral retinal hemorrhages, but her subsequent course is not known. The third patient had redness of the eyeball for two months before vision was affected. Although the eyesight was badly affected and there were numerous hemorrhages in the eyegrounds, he reports normal vision 11 years later.

A fourth patient had just returned from a ride on horseback, three weeks after recovery from pneumonia (*Streptococcus* and influenza organisms were grown from cultures), when she suddenly became confused, semicomatose and delirious. She is said to have had fever, vomiting, ataxia of both hands, in addition to papilledema and loss of vision. There must have been a very diffuse encephalopathy, and occurring so soon after the attack of pneumonia it would appear probable that this was the same source of the inflammatory process in the brain—though without pus formation.

A fifth patient had stinging eyes and photophobia—both suggestive, but not indicative of mild inflammatory origin.

It is worthy of note and perhaps significant that cases with the probable evidence of slight inflammatory character have all been severe, in that they have had hemorrhages and visual defects. However, if these findings are evidences of inflammatory origin, none of them have been pyogenic and none have shown alterations of the cerebrospinal fluid. In none of the remaining cases—excepting the single case of syphilis—has there been any evidence to suggest that the process may be of inflammatory nature.

From six of the 44 cases (13 per cent), therefore, there is evidence of an underlying inflammatory process of some peculiar type. There were pain, redness and swelling of the eyelids—cardinal signs of infection—but in none was there the slightest indication of the character of the infection.

Although a demyelinating process is conceivable (perhaps like that of multiple sclerosis), there is no proof. Moreover, with one exception, there has been but a single insult to the optic nerves, and after this has passed the cure has appeared to be permanent. One would expect repeated and long continued attacks if a demyelination process were the cause.

The Cerebrospinal Fluid Pressure—The pressure of spinal fluid was

measured in nine cases, in only two of which were the readings in the higher reaches of normal—250 and 280. The actual readings were 80, 120, 120, 130, 170, 170, 170, 250 and 280.

In 24 cases, the flow of fluid from the ventricular fluid (tapped for ventriculography) was such as to indicate the absence of intracranial pressure. In two instances it was reported to have been slightly increased.

Cell Count—Cells were counted in 22 cases. The highest count was 12, in the remaining it was 10 (one case) or less.

Globulin Content—The fluid was examined for excess globulin, but in no instance, even the case of syphilis, was there an increased amount.

Roentgenograms and Ventriculography—Roentgenograms of the head were made in nearly all cases, and in none was there a positive or even a suggestive finding. Ventriculograms were made in 37 cases, and since tumors were suspected all injections of air were made through ventricular punctures. All showed normal, symmetrical ventricles, thereby unequivocally excluding intracranial tumors. In two instances, the ventricles were fairly large (both in older persons) and representing, we thought, the normal for those individuals. The ventricles, though small, were, on the whole, somewhat larger than in the group with papilledema and intracranial pressure but without brain tumor.

Vision—Of the 44 cases, 41 complained of disturbance of vision. The most common complaint was dimness or blurring of vision. The degree of visual loss varied from a purely subjective disturbance without actual objective loss in any form to complete blindness. In 14, or approximately one-third of the cases, the visual acuity and visual fields were normal. In eight, there was unilateral loss of vision in some degree, and in 22, or 50 per cent, there was bilateral loss of some degree. In two-thirds of the total number there was visual loss.

In 19 cases, blind spots were enlarged on one or both sides, and in ten the blind spots were normal. In 13, there were scotomata or field defects of varying size.

Eyegrounds—In every case there was papilledema in one or both eyes—42 bilateral and two unilateral. Hemorrhages were present in the eyegrounds in 19 cases (43 per cent), in five, the hemorrhages were unilateral and in 14 bilateral. The hemorrhages were usually petechial, but in two cases they were large and flame-shaped.

Ultimate Results—Thirty-one cases have been traced, some by letters, others have returned for examination. Two are dead, one, 18 months later of chronic encephalitis, which was doubtless the lesion at the time of our examination, the other patient died eight years later following an abdominal operation. Only two of these patients are reported in less than a year after the initial study, seven have gone two years or less, four between two and three years, two between three and five years, nine between five and ten years, and seven more than ten years, the longest 14½ years.

In seeking the ultimate effects upon vision, the original cases have been

divided into four groups. Those with (1) papilledema only, (2) hemorrhages in the eyegrounds, (3) scotomata and enlarged blind spots, and (4) field defects.

Papilledema Only—There were nine cases in this group, and in all the vision has remained normal both subjectively according to the patients' report and objectively in those who have come for examination in the check-up. Five of these are over ten years, the remaining between one and one-half and three and one-half years.

Hemorrhages in Eyegrounds—Of the 13 cases with hemorrhages in the eyegrounds, one is blind and was blind at the time of our first study nine years earlier, a field defect remains in three, and in nine the vision is said to be normal.

The return of visual acuity in several of these patients is most striking. One patient's visual acuity returned from 12/200 to 20/70 (six and one-half years), another from 3/200 and 12/200 to 20/30 in each eye (three years), and another from 10/200 and 80/200 to 20/20 in each eye (six years).

Scotomata and Blind Spots—Of 13 patients who have been followed, nine are now normal, and in four the vision has remained unchanged.

Field Defects—This is the group with the most severe visual changes and with the poorest prognosis. Of 11 cases, the vision in seven has remained unchanged, in one, the vision returned to normal in one eye and is only useful in the other (one and one-half years later). At the time of the original study in the latter patient both eyes were essentially the same, he being practically blind. In the three remaining cases of this group the vision has returned to normal in both eyes. In one of these patients, blind when first seen, the visual acuity and visual fields are normal six years later. In another who was blind in one eye, the visual acuity and fields are again normal two years later.

SUMMARY AND CONCLUSIONS

(1) Forty-four cases of papilledema without intracranial pressure are presented. The underlying etiologic or pathologic basis is unknown, except that two cases of multiple sclerosis and two of encephalitis are included. No evidence of either of these lesions can be found in the remaining cases. A few of the cases appear to follow a mild nonspecific inflammatory process in the eye or lids, but these cases are distinctly in the minority.

(2) Although there is evidence of some intracranial involvement in some cases, in others there is none. Moreover, the papilledema may be unilateral, although it is much more commonly bilateral. On the whole, the pathologic process is decidedly local and any intracranial extension and its effects are usually mild and of little concern. Exceptions to this statement are, of course, the examples of encephalitis and multiple sclerosis.

(3) The condition carries no danger to life, and heals spontaneously in the course of a few weeks or months. No form of treatment is known to be effective. Certainly, all forms of operative intervention are contraindicated.

(4) Women are affected nearly three times as frequently as men. It occurs in all decades of life in about equal frequency, except the second, where it is two and one-half times as common.

(5) The outstanding symptom is loss of vision—usually a blurring at first. Scotomata, field defects and blindness may develop with great rapidity, and may or may not remain. Great defects of vision and visual acuity, even blindness, may disappear and even normal vision may return. Permanent blindness resulted in only one case. Hemorrhages in the eyegrounds occur with great frequency.

(6) There are no changes in the cerebrospinal fluid, the pressure is not increased. Ventriculograms are always normal.

(7) In only one case did the papilledema recur. This was three years after the initial attack and three years ago. On each occasion the vision was seriously defective, but returned almost to normal. The eyegrounds show only slight pallor of the disks. In another case, a dense scar fills the disk and obliterates all of its landmarks.

REFERENCES

- ¹ Dandy, W. E. Intracranial Pressure Without Brain Tumor. Diagnosis and Treatment. *ANNALS OF SURGERY*, 106, 492, 1937.
- ² Bordley, James, Jr. Ocular Manifestations of the Paranasal Sinuses. *Arch Ophthalmol*, 1, No 2, 137, 1921.
- ³ Cushing, H. Accessory Sinus Disease and Choked Disk. *JAMA*, 75, No 4, 236, 1920.
- ⁴ Fuchs. Case of Eye Disturbance in Accessory Sinus Disease. *Lehrbuch der Augenheilkunde*, Ed 10, 766, 1905.
- ⁵ Hajek, H. Kritik des rhinogenen Ursprunges der retrobulbaren neuritis. *Wien klin Wchnschr*, 33, 267, 1920.
- ⁶ Marburg, O. Retrobulbar Optic Neuritis and Multiple Sclerosis (Bibl). *Zeit f Augenh*, 44, 125, 1920.
- ⁷ Oliver, K. S., and Crowe, S. J. Retrobulbar Neuritis and Infection of Accessory Nasal Sinuses. *Arch Otolaryngol*, 6, 503, 1927.
- ⁸ Richardson, S. A. Optic Neuritis Resulting from Hyperplastic Ethmoiditis and Sphenoiditis. *Jour Florida Med Assn*, 9, 22, 1922.
- ⁹ Stark, H. H. Retrobulbar Neuritis, Secondary to Disease of the Nasal Sinuses. *JAMA*, 77, No 9, 678, 1921.
- ¹⁰ Stough, J. T. Choking of Optic Disks in Diseases Other Than Tumor of Brain. *Arch Ophthalmol*, 8, 821, 1932.
- ¹¹ Walker, C. B. Retrobulbar Neuritis and Multiple Sclerosis. *California and Western Med*, 34, No 1, p 5, No 2, p 83, 1931.
- ¹² Weill, G. Relationship Between Inflammation of Posterior Sinuses and Disease of Nervus Opticus. *Arch Ophthalmol*, 1, 307, 1929.
- ¹³ White, L. E. Blindness from Teeth, Tonsils and Accessory Sinuses. *Boston Med and Surg Jour*, 192, 64, 1925.

HURTHLE CELL TUMORS OF THE THYROID

J D MARTIN, JR., M D, AND D C ELKIN, M D

ATLANTA, GA

FROM THE DEPARTMENT OF SURGERY, EMORY UNIVERSITY, ATLANTA, GA

IN A HURTHLE CELL TUMOR of the thyroid there is supposed to be a proliferation of cells similar to those described originally by Hurthle, in 1894. These cells are considered normal constituents of the thyroid and capable of reproducing thyroid tissue when necessary. This opinion is not universally accepted but it gives an insight into the type of structure that exists.

There are three opinions regarding the histogenesis of these tumors. The arguments in favor of each are equally convincing but as yet they have not been proved. It was regarded by Langendoiff, and others, that the tumors arose from the cells first noted by Baber,¹ in 1874. These cells were later termed "*proto plasmischen Zellen*" by Hurthle,² in 1894. They are thought to be para- or interfollicular cells, the function of which will be discussed later. In 1907, Sophia Getzowa³ advanced the theory that these lesions had their origin from the rests of the primary postbranchial body or lateral thyroid anlage. The third opinion is that these tumors arise from normally located or ectopic parathyroid cells.

The morphologic characteristics have been thought to resemble the cells of the liver, parathyroid and adrenal cortex. The primary cells are large polyhedral, eosinophilic, granular structures, measuring from 15 to 20 microns, and containing chromatin in clumps. These cells, as is noted, are large, compactly arranged, and form small alveoli. The lumina are usually small with an absence of the normal thyroid arrangement, which in turn gives the tissue a solid appearance. The gross appearance may be that of a discrete, well encapsulated structure. On the other hand, there may be a diffuse invasion with the tumor cells surrounding normal tissue.

The gross and microscopic structure of the fetal adenoma resembles more the Hurthle cell tumors than other thyroid tumors. The fetal adenoma is composed of small cell alveoli, but the epithelial cells are somewhat smaller and more hyperchromatic. There is a distinct difference in the stroma. In fetal adenoma there are large areas of clear, loose connective tissue, whereas, in Hurthle tumors, the fibrous tissue is less.

A differentiation of the malignant types is not always easy, but the same criteria are applicable as in other types.⁴ The morphology of the cell is not as significant as other characteristics, such as relationship to alveoli and gland. The invasion of the blood vessels is by far the most frequent characteristic of malignancy of the thyroid. There may be an involvement within the capillaries and larger veins with thrombi formation. Wilensky and Kauf-

man,⁵ in 1938, noted that four cases had been recorded as benign and six as malignant. It is reasonable to believe that many of both types have been encountered but never considered and reported as such. Therefore, we are reporting three additional cases, one of which is definitely malignant and the other two are questionable.

CASE REPORTS

Case 1—S. N., Negro, female, age 46, was admitted to the Emory University division of Grady Hospital, September 3, 1937, complaining of enlargement of the neck, which had been present for ten years. She had had evidence of thyrotoxicosis two years prior to admission. There had been a slight loss of weight. The basal metabolism was normal. The left lobe of the thyroid was nodularly enlarged to about 4 cm in diameter. It was freely movable and firm, but not hard. The physical examination was otherwise normal.



FIG 1.—Case 1. Showing orderly arrangement of small alveoli containing a few large cells. There are scattered areas of colloid within the large cystic spaces. (Low power.)

On September 7, 1937, a nodular mass was removed from the left lobe of the thyroid, which extended 2 cm beneath the sternum. The tumor was irregular but well encapsulated, measuring 3.5 x 4 cm and involving practically the entire left lobe of the thyroid. On cut section three distinct nodules were present. Each was surrounded by a thick fibrous capsule. The surface was homogeneous, pale yellow in color. There was no resemblance to normal thyroid structure.

Histologic examination revealed an extremely cellular structure with numerous islands of compact epithelial cells attempting to form acini. The basement membrane was fairly distinct. The epithelial cells were large and granular in appearance. The alveoli were diminished in size and contained a small amount of colloid. The entire area was extremely vascular. *Diagnosis:* Benign Hurthle cell tumor of the thyroid.

Since removal, there has been no evidence of recurrence of disease.

Case 2—J. A., Negro, female, age 38, was admitted to the Emory University division of Grady Hospital, November 9, 1936. The chief complaint was an enlargement of the thyroid. This had been present for five years as a small nodular mass in the right side of the neck. The patient had had frequent attacks of sore throat and

HURTHLE CELL TUMORS OF THYROID

difficulty in swallowing for the two months prior to admission. She had marked dysphagia and dyspnea, particularly on lying flat in bed.

Physical examination showed a well developed and nourished Negro female. The right lobe of the thyroid was moderately enlarged, and was displacing the trachea to the opposite side. The remainder of the physical examination was normal except for a fibroid tumor of the uterus.

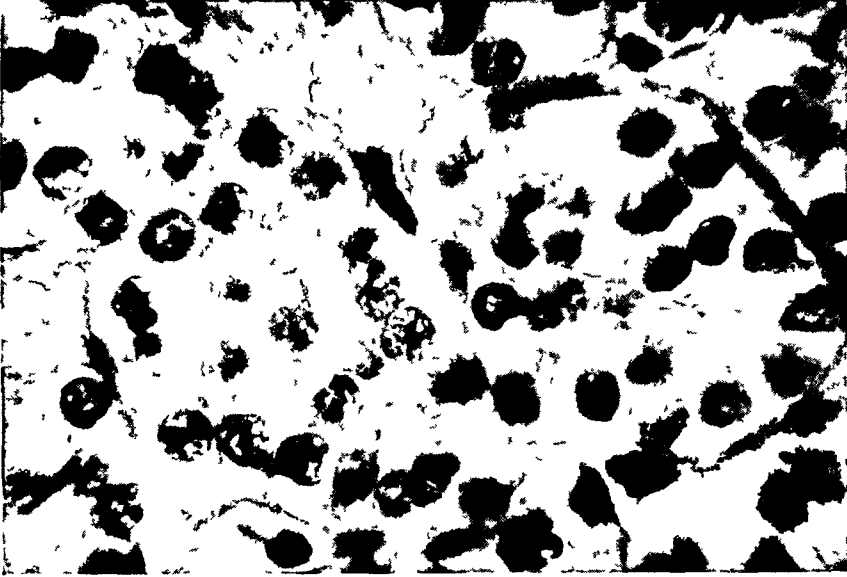


FIG 2—Case 1. Presenting compact small alveoli with large cells. The nuclei are polyhedral in shape and contain much granular material. The basement membrane is very prominent. (High power.)

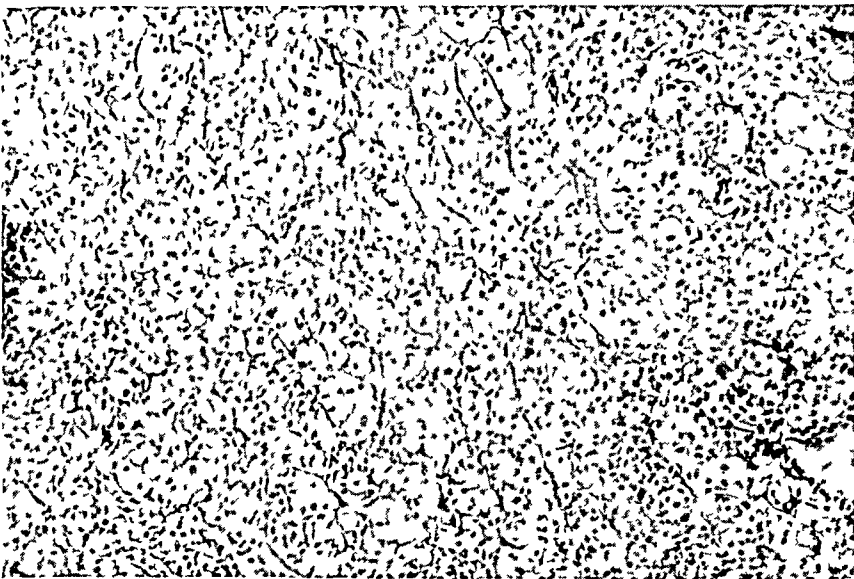


FIG 3—Case 2. Presenting typical large cells forming small alveoli. There are many vacuolated areas throughout with loose fibrous septa separating the alveoli. (Low power.)

Basal metabolism on admission to the hospital was plus 22. After ten days' bed rest the metabolism was plus five. Blood chemistry was normal, including blood cholesterol. The clinical diagnosis was mild toxic adenoma.

Operation was performed, November 14, 1936, which revealed an enlargement of the right lobe. This was nodular and measured 4 cm. in diameter and 6 cm. in length. The remainder of the thyroid was apparently normal.

Pathologic examination revealed a mass 6x3x3 cm. The surface was irregular and surrounded by a thick capsule. On cut section the tumor was a grayish-yellow with dense fibrous trabeculae dividing the mass. The substance was homogeneous between these areas. There was an absence of the normal colloidal appearance.

Histologic examination revealed many cystic spaces lined by a flat type of epithelium. Between these cystic areas there was a different cellular structure which consisted of



FIG 4—Case 2 Showing the large polyhedral shaped cells with prominent granular nuclei (High power)

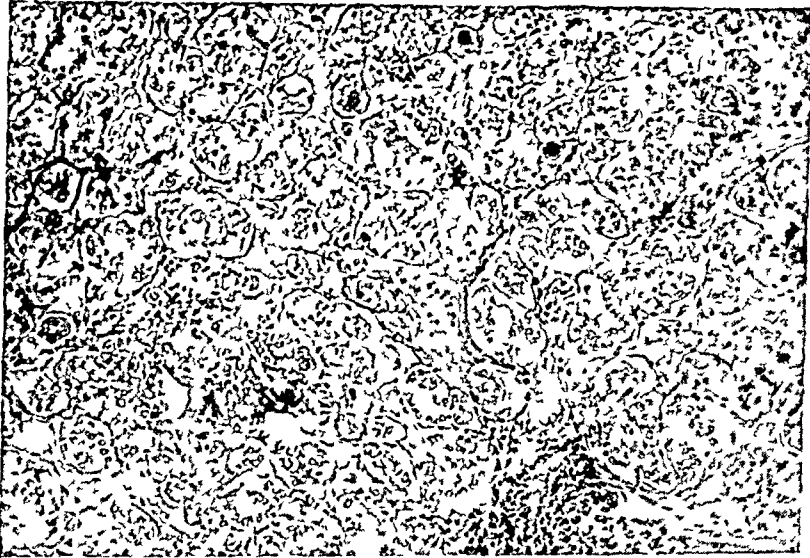


FIG 5—Case 3 An adenocarcinoma which presents a cellular structure composed of large cells forming irregular sizes and shapes of alveoli (Low power)

large pale cells and contained considerable granular material. The nuclei were large, granular and ovoid in shape. There was very little stroma and no evidence of hyperplasia. *Diagnosis* Hurthle cell tumor.

There has been no evidence of recurrence of the disease.

Case 3—E. H., Negro, female, age 54, was admitted to the Emory University division of Grady Hospital, April 27, 1937, complaining of hoarseness and enlargement of the glands of the neck. Patient stated that, for about 3 years, she had noticed two

HURTHLE CELL TUMORS OF THYROID

small nodules in the lower part of the right side of her neck. These remained unchanged until about six months before admission, when they began to increase in size and to cause difficulty in breathing. Soon afterwards she became hoarse and had continued so until admission. She had lost 25 pounds in weight over a period of two years.

Physical examination revealed numerous nodules adjacent to the thyroid cartilage and extending on the inner side of the right sternomastoid muscle accompanying the internal jugular vein. There were five discrete nodules along this area. The thyroid gland was enlarged, irregular in shape and slightly tender. The remainder of the physical examination and laboratory findings were negative.

On May 1, 1937, a small nodule measuring 2 cm in diameter was removed for diagnosis. On cut section the surface was roughened and had a yellowish-white color.

Microscopic examination revealed a thickened capsule enclosing large epithelial cells which contained hyperchromatic nuclei. These cells were attempting to form regular acini in which there were small amounts of colloid. The acini were small in

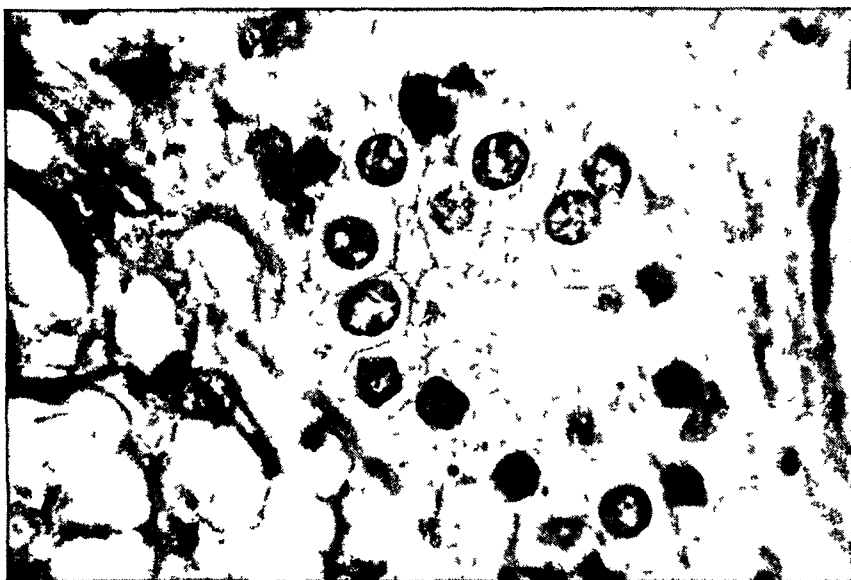


FIG 6—Case 3 Presenting typical large epithelial cells with very prominent cell walls. There are many chromophobic vacuoles and mitoses (High power)

type and the basement membrane was indistinct. The nuclei were very granular and contained many mitotic figures. The stroma consisted of loose connective tissue which was surrounded by many thick-walled blood vessels. An occasional foreign body type of giant cell was seen. *Diagnosis:* Malignant Hurthle cell tumor of the thyroid.

At operation, May 8, 1937, the sternomastoid muscle and the internal jugular vein on the right side were removed with accompanying lymph nodes. The right lobe of the thyroid was found diseased, but the left was apparently normal. The right lobe consisted of an extremely nodular and hardened gland which was densely adherent to all the surrounding structures. The right lobe measured 4x3 cm. On cut section there were many large cystic spaces which contained greenish gelatinous material. Between these areas was a solid structure which was pale in color. There was no evidence of normal thyroid tissue in the right lobe.

Histologic section was similar to that seen in the previously examined lymph node. The cells were large and formed irregularly shaped small acini. The nuclei were prominent and contained considerable granular material. Mitoses were numerous. There were scattered areas of calcification through the entire lobe. *Diagnosis:* Malignant Hurthle cell tumor of the thyroid.

The patient recovered from this procedure without incident. Roentgenograms of

the long bones were negative for metastases. She was given postoperative irradiation over the neck and the region of the thyroid. There has been no evidence of recurrence of the tumor.

Discussion—In order to evaluate the various theories regarding the histogenesis of these tumors, it is first necessary to review some of the concepts of development and function of the thyroid.

Since the description of the formation of the follicle by the early investigators, namely, Baber and Hurthle, much difference of opinion has arisen concerning the method of formation and the function of the follicles with particular reference to the relation of the colloid.

Hurthle² believed that there were two types of interfollicular cells. The difference was mainly in the size and the content of the protoplasm. The small cells were usually round in shape, whereas the large ones were seldom so. In the development a group of the larger cells came together and formed alveoli. These cells are probably the same as Baber's parenchyma cells, which are large interfollicular cells, rich in protoplasm, finely granulated and with a single large nucleus. Baber¹ first thought the cells were outside of the follicles and that the epithelial wall was flattened and moved aside, thus allowing the cells to finally reach the interior of the follicle and become a part of the colloid content. Hurthle, however, failed to concur in this opinion as to the fate of these cells.

Zechel^{6, 7} believed that there were two types of cells. The first were the epithelial cells which were the most prevalent type. The second were the large cells which were located in the interfollicular spaces. The function of the latter was the formation of new follicles, production of colloid and the possible inception of follicular destruction.

Nonidez¹ agreed with the occurrence and formation of parafollicular cells but believed they are separate from the glandular epithelium. This opinion was strengthened by Takagi, in 1922. He was able to show a difference in the staining characteristics of the cells.

Marine and Lenhart⁸ considered the follicles to be the unit of structure, which were round or oval closed spaces lined by cuboidal epithelium. Williamson and Pearse⁹ thought the thyroid was divided by interstitial tissue into lobules. These lobules were thought to be closed by a meshwork of fibro-elastic tissue which supports the endothelium of the lymphatic sinusoids. This was an expansion of the intralobular lymphatics. The coiled columns of epithelium were located within the sinusoids. The columns of epithelium were surrounded by a peculiar ladder-like plexus of capillaries.

Gale Wilson¹⁰ studied normal and abnormal thyroids and was unable to find such a unit structure as Williamson and Pearse. She considered, also, the process of vesiculation to be the means whereby the continuity of the follicles was maintained. The follicles are thought to be separate, and not to have individual lobules bathed by lymphatics. These developmental and anatomic beliefs aid in supporting and furnishing evidence for the interfollicular theory of formation.

Getzowa¹ presumed that the cysts seen in the atrophied thyroids of cretins and idiots were probably rests of the primary lumen of the post-branchial body. It was also concluded that the histologic structure of the cell masses is not comparable to the thyroid or parathyroid as they are composed of large protoplasm-rich cells and often contain cilia in the small lumen. The author believed these masses to be remnants of the glandular parenchyma of the postbranchial cell masses. These cells were similar to, if not identical with, the epithelial cells of the large cell, small alveolar tumors described by Langhans.

Eisenberg and Wallestein¹¹ were firm believers of the parathyroid theory of formation of these tumors. It was thought that the cells arose from parathyroid cells either within or outside the thyroid. The belief was based on the description of the principle and chief cells of the parathyroid made by Welsh, in 1898. The similarity of the oxyphilic cells described by Hurthle was noted by this investigation.

There is no unanimity of opinion concerning the origin of these tumors, but the histologic structure is well understood. Ewing's¹² description explains the fundamental structure in that they are "small, well formed alveoli lined by one or more layers of irregular cells. Some are clear, cuboidal or cylindrical or irregularly polyhedral. Others are large, sometimes giant size, finely granular eosinophilic, and opaque, resembling granular suprarenal or liver cells. The nuclei are small and vesicular in type with prominent nucleoli. Rather numerous globules of colloid are usually present and the original structure reappears in metastasis."

Ewing classifies these tumors as "small alveolar, large cell adenocarcinoma," as Langhans originally did. Contrary to the belief of many, he considers all of these tumors malignant.

There is no essential difference in the course of these tumors and similar ones of the thyroid. The important feature is the recognition of the malignant and benign types. There has been inadequate investigation to determine whether these malignant growths begin from benign lesions or if these types develop as separate tumors, as in other types of adenomata.

The treatment should be early surgical removal. It is obvious that diagnosis of this type of thyroid will not be made until after removal. It is frequently impossible to recognize the malignancies, as the one reported here was not seen until regional metastasis had occurred.

SUMMARY

(1) Three cases of so-called Hurthle cell tumor of the thyroid are reported. Two are classified as benign and one as malignant.

(2) The possible origin of these tumors is presented. As yet, there is no unanimous opinion regarding their histogenesis.

(3) The clinical course and treatment of these lesions are similar to other thyroid adenomata, both the benign and malignant types.

REFERENCES

- ¹ Nonidez, Jose F The Parenchymatous Cells of Baber, the Protoplasmeichen Zellen of Hurthle and the Parafollicular Cells of the Mammalian Thyroid Anat Rec, 50, 131, May, 1933
- ² Hurthle, K A Study of the Secretory Process of the Thyroid Gland Arch f d Ges Physiol, 56, 1894
- ³ Getzowa, S The Parathyroid Gland, Intrathyroid Cell Masses of the Same and Rest of the Postbranchial Body Virchows Arch f Path Anat u Physiol, 188, 1907
- ⁴ Graham, A Malignant Epithelial Tumors of Thyroid Surg, Gynec, and Obstet, 39, 781-791, 1924
- ⁵ Wilensky, A, and Kaufman, P Hurthle Cell Tumor of Thyroid Gland Surg, Gynec, and Obstet, 66, 1, January, 1938
- ⁶ Zechel, Gustav Cellular Studies on the Thyroid Gland Surg, Gynec, and Obstet, 54, 1-5, 1932
- ⁷ Zechel, Gustav Observation on the Follicle Cycle and on the Presence of the Macrothyrocyte in the Human Thyroid Anat Rec, 56, May, 1933
- ⁸ Marine, David, and Lenhart, C H The Pathological Anatomy of the Human Thyroid Arch Int Med, 7, 506-535, 1911
- ⁹ Williamson, G S, and Pearse, I H The Structure of the Thyroid Organ in Man Jour Bact and Path, 26, 1923
- ¹⁰ Wilson, Gale The Thyroid Follicles in Man, the Normal and Pathological Configuration Anat Rec, 37, 31-61, November, 1927
- ¹¹ Eisenberg, A A, and Wallerstein, Harvey Hurthle Cell Tumor Arch Path, 13, 716-724, 1932
- ¹² Ewing, James Neoplastic Disease 3rd Ed, p 952, W B Saunders Co, Philadelphia

RETROPHARYNGEAL AND LATERAL PHARYNGEAL ABSCESES

AN ANATOMIC AND CLINICAL STUDY

MANUEL GRODINSKY, M D

OMAHA, NEB

FROM THE DEPARTMENTS OF SURGERY AND ANATOMY, UNIVERSITY OF NEBRASKA, COLLEGE OF MEDICINE, OMAHA, NEB

RETROPHARYNGEAL and lateral pharyngeal abscesses have been recognized and described under various terms (pharyngeal abscess, pharyngomaxillary abscess, postpharyngeal abscess, abscess of the neck, phlegmon of the neck, pterygomaxillary abscess, *etc*) for a long time. According to Holmes (1907), Galen referred to a case of retropharyngeal abscess. Allin (1851) stated that the earliest mention of abscess behind the pharynx is to be found in the works of Plateus, in 1625. Horner (1818) described a case starting from ulcerations of the tonsil. Abercrombie described three cases, in 1819, and Fleming two cases, in 1850. Among other early reports and discussions were those of Taylor (1846), Henoch, in 1850 (Holmes, 1907), Pretty (1858), Bokai, Sr, in 1876 (Holmes, 1907), Chiene (1877), Elliot (1879), Smith (1879), Savoy (1880), Allen (1881), Cheyne (1881), Agnew (1882), McCoy (1882), Sands, (1882), Tyler (1882), Parker (1883), de Blois (1885), Clutton (1887), Burckhardt (1888), Hawkins-Ambler (1891), Belg (1894), Bokai, Jr, in 1896 (Holmes, 1907), and Koplik (1896).

Morse (1903) discussed the etiology and pathologic anatomy in detail. Similar descriptions were made by Meierhof (1905), Waugh (1906), Sheedy (1912), Badgerow (1912), Alexander and Montague (1913), McKenzie (1915), Fulkerson (1916), Richardson (1920), Waldapfel (1928), and Beck (1932). Travers (1902), Palmer (1933), and Salinger and Pearlman (1937) emphasized secondary hemorrhage from erosion of the large vessels of the neck.

Drainage of the superior and posterior mediastinum by cervical and thoracic approaches was described by Nasiloff (1888), Quenu and Haitmann (1891), Bryant (1895), Rehn (1898), Heidenhain (1899), Von Hacker (1901), Guadiani (1916), Lerche (1921-1924), and Lilienthal (1923). Dean (1919) described a method of external drainage for abscesses secondary to caries of the vertebrae. Mosher (1920 and 1929) discussed the fasciae and fascial compartments of the neck, emphasized the importance of thrombosis of the internal jugular vein and described incisions for drainage. Furstenberg (1929) described the fascial layers and compartments in the neck, and discussed the routes of spread from the nose and throat to the posterior mediastinum. He also discussed cervical (collar) and thoracic (dorsal) mediastinotomy. Kana-vel (1922) described two cases treated by external incision. Numerous other articles, mostly case reports, have been found in the literature.

In a previous article (Grodinsky and Holyoke, 1938), a description of the fasciae of the head, neck and adjacent regions has been given based on the

Figures 1 to 3 inclusive, are diagrammatic drawings based upon data of dissections, sections and injections of adult and fetal material

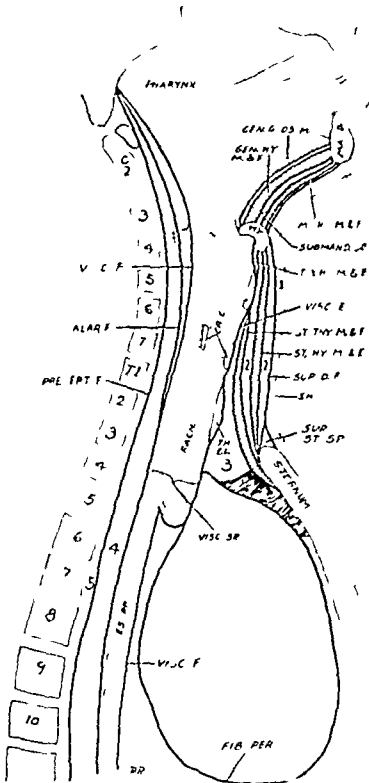


FIG 1—Diagrammatic drawing of fasciae of head and neck in midsagittal section

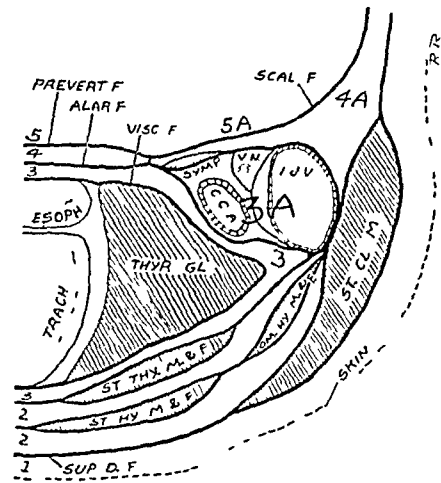


FIG 2—Diagrammatic drawing of fasciae of neck. Transverse section up proximately at the level of the 6th cervical vertebra

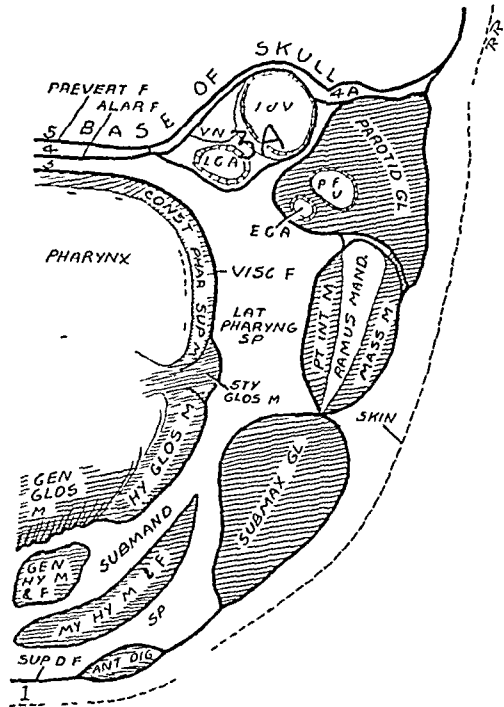


FIG 3—Diagrammatic drawing of fasciae of the head and neck. Oblique anteroposterior section showing the relation of the submandibular space to the lateral pharyngeal space and spaces 3 and 4

KEY TO ABBREVIATIONS ON ILLUSTRATIONS

ALAR F—Alar fascia AX SP—Axillary space ARYT—Arytenoid cartilage
A AOR—Ascending aorta AZ V—Azygos vein BR PL—Brachial plexus CLAV—
Clavicle COROC—Coracoid process CRIC—Cricoid cartilage C C A—Common
carotid artery CONST PHAR SUP M—Superior pharyngeal constrictor muscle
D AOR—Descending aorta D D PECT F—Deep layer of deep pectoral fascia

study of 75 adult cadavers and five full term fetuses by dissection, injection and section methods. In a second article (Giodinsky, 1938), this description was reviewed with special reference to its application to the clinical entity known as Ludwig's angina. It is my purpose in this article to review this anatomic description with special reference to retropharyngeal abscess and to discuss the clinical picture and treatment.

ANATOMY—Layers of Fasciae The superficial fascia is a continuous sheet of fatty tissue extending from the head and neck into the regions of the thorax, shoulders and axillae. In the neck it is a moderately loose layer containing the platysma muscle in its deep portion. In the face the superficial fascia is very adherent to the overlying skin and contains the muscles of expression in its deep portion.

The superficial layer of deep fascia crosses the anterior triangle of the neck, splits to form the sheath of the sternocleidomastoid muscle, crosses the posterior triangle, splits to form the sheath of the trapezius muscle, and finally attaches to the spines of the vertebrae in the midline posteriorly. In the midline anteriorly, it splits to form the suprasternal space of Burns, its anterior and posterior leaflets attaching to the corresponding margins of the sternum. Lateral to the sternum, it is attached inferiorly to the clavicle, acromium, and spine of the scapula. A corresponding layer, the superficial layer of deep pectoral fascia, then continues from the anterior inferior surface of the clavicle

DELT M—Deltoid muscle DIG ANT M—Digastric muscle, anterior belly DIG POST M—Digastric muscle, posterior belly E C A—External carotid artery EPIGL—Epiglottis ESOPH—Esophagus EUST TUBE—Eustachian tube GEN GLOS M—Genioglossus muscle GEN HY M—Geniohyoid muscle GLOT—Glottis HY—Hyoid bone HY GLOS M—Hyoglossus muscle I C A—Internal carotid artery I J V—Internal jugular vein L LUNG—Left lung LEV VEL PAL M—Levator veli palatini muscle LAT PHARYNG SP—Lateral pharyngeal space MAND—Mandible MASTIC SP—Masticator space MAST PROC—Mastoid process MAX S—Maxillary sinus MY HY M—Mylohyoid muscle OCCIP BONE—Occipital bone OM HY M—Omohyoid muscle P A—Pulmonary artery PAROT GL—Parotid gland PECT MAJ M—Pectoralis major muscle P F V—Posterior fascial vein PREVERT F—Prevertebral fascia PT INT M—Internal pterygoid muscle PT EXT M—External pterygoid muscle PHR N—Phrenic nerve PAR PL—Parietal pleura R LUNG—Right lung SCAL F—Scalenus fascia SCAL ANT M—Scalenus anterior muscle SCAL MED M—Scalenus medius muscle SCAL POST M—Scalenus posterior muscle ST—Sternum SCAP—Scapula SUP D F—Superficial layer of deep fascia SUP D PECT F—Superficial layer of deep pectoral fascia SUBMAND SP—Submandibular space SUP ST SP—Suprasternal space SUBMAX GL—Submaxillary gland S V C—Superior vena cava ST CL M—Sternocleidomastoid muscle ST HY M—Sternohyoid muscle ST THY M—Sternothyroid muscle STY HY M—Stylohyoid muscle STY GLOS M—Styloglossus muscle STY PHAR M—Stylopharyngeus muscle SUBCLAV M—Subclavius muscle SYM—Sympathetic trunk TEMP M—Temporalis muscle THY—Thyroid cartilage THY GL—Thyroid gland THYM GL—Thymus gland TRACH—Trachea TRANS F—Transversalis fascia TEN VEL PAL M—Tensor veli palatini muscle TRAP M—Trapezius muscle THY HY M—Thyrohyoid muscle VISC F—Visceral fascia VISC PL—Visceral pleura VISC SP—Visceral space V N—Vagus nerve ZYG—Zygoma

around the pectoralis major muscle, and at the lateral inferior border of this muscle becomes the deep axillary fascia, which crosses the axilla and splits to form the sheath of the latissimus dorsi muscle (Figs 1, 2, 6 and 7)

Superiorly the superficial layer of deep fascia attaches to the hyoid bone, and proceeds across the submental and submaxillary triangles (submandibular space) It fuses with the sheath of the anterior belly of the digastric muscle, although the two layers may be easily separated It also becomes attached to the sheaths of the stylohyoid muscle and the posterior belly of the digastric muscle, and then splits to form the capsule of the submaxillary salivary gland This is a completely closed capsule which attaches superiorly by two slips to the superficial and deep margins of the body of the mandible The anterior belly of the digastric, the mylohyoid, the geniohyoid, the genioglossus, and the hyoglossus have independent sheaths with bony attachments at the attachments of these muscles (Figs 1, 3, 5 and 9)

Figures 4 to 9 inclusive are line drawings made on bleached photographs of serial sections of human material

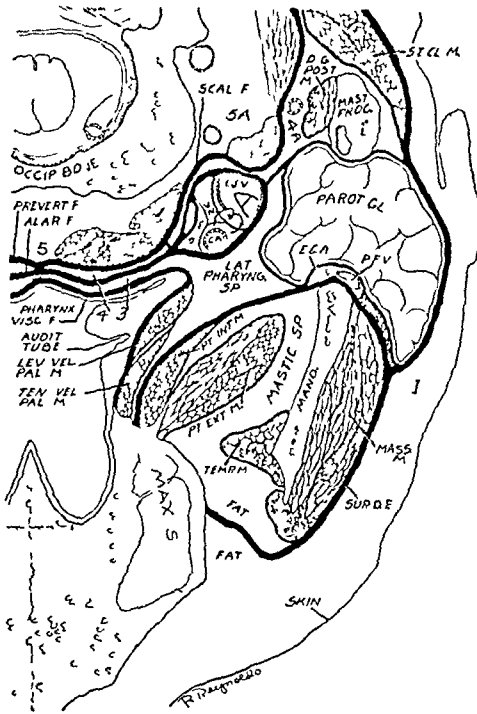


FIG 4—Transverse section of adult cadaver at level of hard palate Superior view

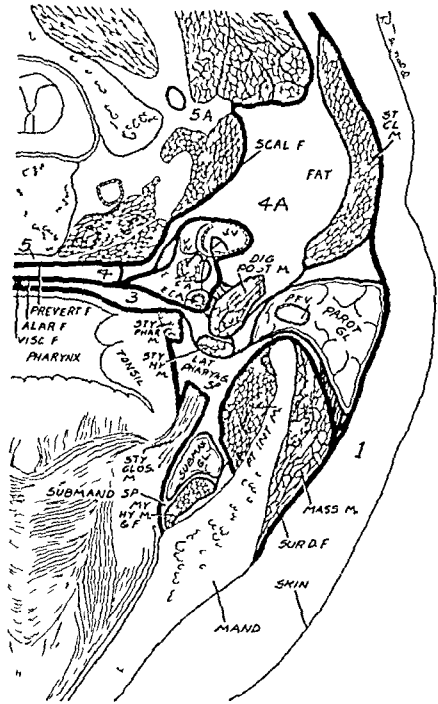


FIG 5—Transverse section of adult cadaver through the tongue and the palatine tonsil Superior view

Between the angle of the jaw and the anterior border of the sternocleidomastoid muscle, the superficial layer of deep fascia splits to form the capsule of the parotid gland, which in our experience is complete on all sides From the body of the mandible, the superficial layer of deep fascia extends superiorly to form the sheath of the masseter muscle and attaches to the zygoma above It then continues superiorly over the temporal muscle as the outer layer of deep temporal fascia At the anterior and posterior borders of the masseter, it passes around the corresponding borders of the ramus of the mandible and

RETRO- AND LATERAL PHARYNGEAL ABSCESSSES

becomes continuous with the sheaths of the pterygoid muscles, thus completing the walls of the masticator space (see below) (Figs 3, 4, 5 and 9)

The middle layer of deep fascia consists of three subdivisions. The *sternohyoid-omohyoid layer*, the *sternothyroid-thyrohyoid layer* and the *visceral layer*. The former is continuous across the midline anteriorly, forms the sheaths of the sternohyoid and omohyoid muscles, and attaches to the deep surface of the sternocleidomastoid sheath, where it forms a pulley between the anterior and posterior bellies of the omohyoid muscle. Superiorly it is attached to the hyoid bone and, more laterally, to the overlying superficial layer of deep fascia and underlying sternothyroid-thyrohyoid layer along the superolateral border of the anterior belly of the omohyoid muscle. Likewise, in the posterior triangle, it is attached along the superolateral border of the posterior belly of the omohyoid muscle. Inferiorly this layer is attached to the sternum, clavicle, and scapula. A corresponding layer, the deep layer of deep pectoral fascia, starts at the clavicle, splits to form the sheath of the subclavius muscle, becomes the costocoracoid membrane, splits to form the sheath of the pectoralis minor muscle, and becomes the suspensory ligament of the axilla which runs into the axillary fascia. (Figs 1, 2, 6 and 7)

The *sternothyroid-thyrohyoid layer* crosses the midline anteriorly, splits to form the sheaths of the muscles indicated in the name, and runs laterally into the deep surface of the sternocleidomastoid sheath, fusing here with the carotid sheath. Inferiorly it attaches to the sternum and clavicle. Superiorly it attaches to the thyroid cartilage and hyoid bone, more laterally to the superficial layer of deep fascia and the sternohyoid-omohyoid layer superficially, and the carotid sheath deeply. (Figs 1, 2, 6 and 7)

The *visceral fascia* completely surrounds the thyroid gland, trachea and esophagus. Superiorly it extends to the base of the skull on the posterior side, and to the thyroid cartilage and hyoid bone on the anterior and lateral sides. Inferiorly, at the root of the neck, it fuses with the alar fascia of the anterior wall of the carotid sheath, and becomes continuous with the fibrous pericardium covering the heart and great vessels of the thorax. It also continues inferiorly as the covering of the thoracic portion of the trachea and esophagus. (Figs 1 to 8)

Deep Layer of Deep Fascia—There are two main subdivisions. The alar

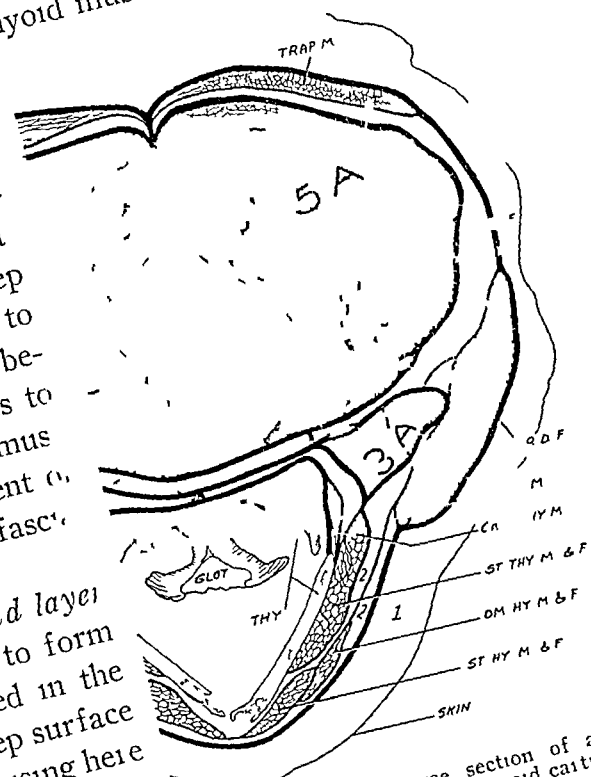


FIG 6—Transverse section of adult cadaver at the level of the thyroid cartilage Superior view

and *prevertebral* fasciae, including the continuations of the latter, *e g*, scalenus, transversalis, and Sibson's fasciae

The *alar fascia* extends across the midline posterior to the pharynx, esophagus and visceral fascia, and fuses with the prevertebral fascia at the tips of the transverse processes, to which both these layers are attached. It then passes anterolaterally to form the medial wall of the carotid sheath, fusing with the sternothyroid layer and the deep surface of the sternocleidomastoid sheath. It also forms the posterior and lateral walls of the carotid sheath, again fusing with the deep surface of the sternocleidomastoid sheath and thus forming a complete sheath of alar fascia, the carotid sheath. Posteriorly, between the transverse processes, the alar fascia extends from the base of the skull to about the level of the seventh cervical vertebra, where it becomes intimately fused with the visceral fascia (Figs 1 to 8)

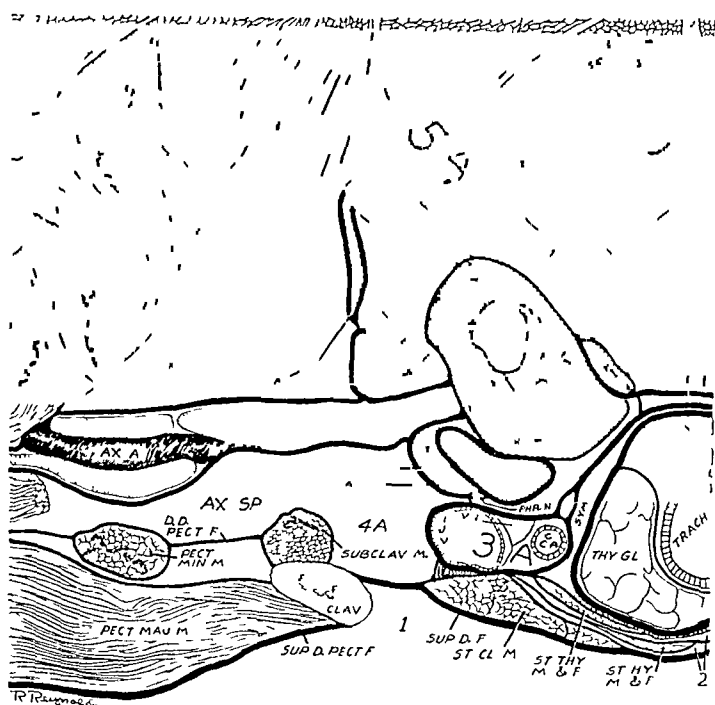


FIG 7—Transverse section of adult cadaver through the root of the neck Superior view

The *prevertebral layer* lies just anterior to the bodies of the vertebrae from the base of the skull to the coccyx. In the neck, it extends laterally to the tips of the transverse processes where it is fused both to these processes and to the alar fascia. Lateral to the transverse processes, it becomes the scalenus fascia which forms the sheaths of the scaleni, splenius capitis, levator scapulae and the other deep muscles of the back of the neck, and finally attaches to the spines of the vertebrae. Inferolaterally the scalenus fascia, after giving origin to the axillary sheath enclosing the axillary vessels and brachial plexus, attaches to the first and second ribs. In the thoracic and abdominal regions, the lateral extension of the prevertebral fascia becomes the extrapleuroperitoneal or transversalis fascia. Over the dome of the pleura, it is identical with the layer often described as Sibson's fascia (Figs 1 to 8)

Fascial Spaces Superficial Space 1—This is the potential space between the skin and deep fascia, that is, within the superficial fascia. It is the seat of superficial cellulitis and is continuous from region to region, in this case from head to neck and trunk. In the neck it may be subdivided into superficial and deep portions by the platysma muscle, both divisions being fairly loose and allowing rather large accumulations of fluids (Figs 1 to 7, and 9).

The deep fascial spaces may be considered under two headings. Those of the *infrahyoid* region and those of the *suprahyoid* region. For convenience we have roughly divided the infrahyoid spaces into those of the anterior and posterior triangles, the former being designated by numerals and the latter by corresponding numerals followed by the letter "A."

Infrahyoid Spaces Space 2—This is the potential space between the superficial layer of deep fascia and the deep layer of the sternothyroid-thyrohyoid sheath. It contains, therefore, the sternohyoid-omohyoid muscles with their sheaths and the sternothyroid-thyrohyoid muscles with the anterior layer of their sheaths. The extent of the space was demonstrated by injections of gelatin colored with India ink, as well as by study of dissections and sections. It is continuous across the midline and is blind laterally where the sternohyoid and sternothyroid layers fuse to the deep surface of the sternocleidomastoid sheath. It is also blind superiorly at the hyoid bone, superolaterally along the superolateral border of the anterior belly of the omohyoid, and inferiorly at the sternum and clavicle. The most frequent extensions of injected masses from this space were along the pulley of the omohyoid to Space 2A, superficially into Space 1, and deeply into Space 3 (Figs 1, 2, 6, 7 and 9).

Space 2A—This space, between the superficial layer of deep fascia and the sheath of the posterior belly of the omohyoid muscle, is blind anteriorly at the pulley, posteriorly at the insertion of the omohyoid (posterior belly), posterosuperiorly along the posterosuperior border of that muscle, and inferiorly at the clavicle. The most common extensions from this space were along the pulley into Space 2, and into Spaces 1 and 4A (Fig 7).

Space 3—This is the potential space between the visceral fascia on the one hand, and the sternothyroid layer, carotid sheath and alar fascia on the other. It thus has anterior, lateral, and posterior portions, all continuous. On the posterior side, it extends from the base of the skull to the level of the seventh cervical vertebra, where it is shut off by the close fusion of the visceral and alar layers. On the anterior side, it extends from the thyroid cartilage to the upper border of the arch of the aorta (fourth thoracic vertebra), where it is shut off by dense adhesions between the fibrous pericardium and the sternum. Laterally this space is blind at the root of the neck, where there are dense adhesions between the alar and visceral fasciae around the inferior thyroid arteries. Injected masses tended to remain localized within this space (3) but, when spread did occur, it was usually into Spaces 2 and 4, and inferiorly into the superior mediastinum slightly lower than the normal limits of the space. This is of special importance in retropharyngeal abscess. Retropharyngeal abscess may thus be confined within the visceral space (between the pharyngeal wall and the visceral fascia) or within Space 3 (between the

visceral and alar fasciae), the extension from the nose and throat occurring by lymphatics or direct continuity. Space 3, as we shall see, is directly continuous with the lateral pharyngeal or pharyngomaxillary space. However, retropharyngeal abscess may also involve Space 4 (see below) either by direct lymphatic extension from the nose and throat or by extension through the alar fascia from Space 3 (Figs 1 to 7).

Space 3A—This is the potential space within the carotid sheath. Primary injections into this space were usually limited closely to the region of injection, but in some cases extended as high as the hyoid bone and as low as the root of the neck, beyond which levels the close adherence of the sheath to the

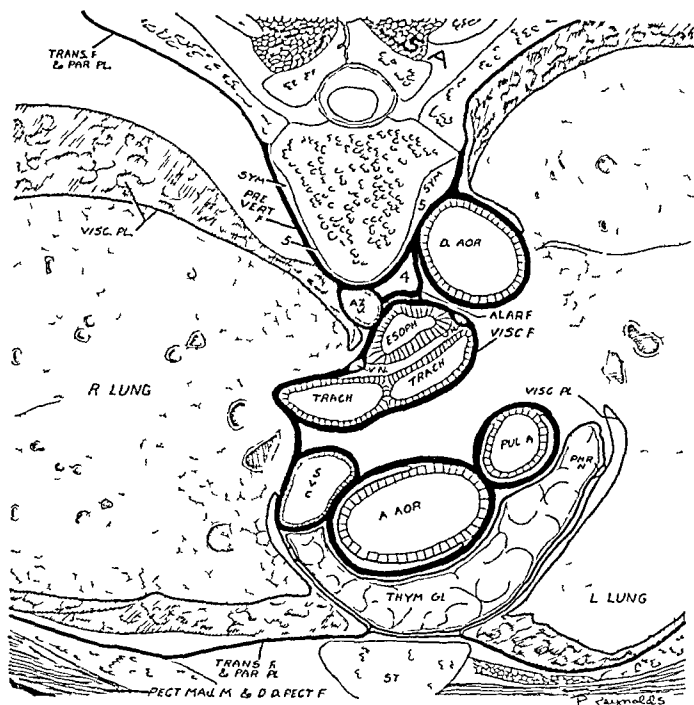


FIG 8—Transverse section of adult cadaver through the superior mediastinum. Superior view.

contained structures made further spread impossible. The space therefore bears little relation to infections of the head and neck except those associated with thrombosis within the internal jugular vein and with the lymph nodes lying within the sheath. According to Mosher (1920 and 1929), thrombosis of the internal jugular vein occurs either by primary extension of infected emboli from the veins of the nose and throat where retropharyngeal abscess begins, or secondary to adenitis and paradenitis of the retropharyngeal, lateral pharyngeal (deep parotid) or pendent groups of lymph nodes which drain the nose and throat. Waldapfel (1928) demonstrated the presence of thrombi in the tonsillar veins, but stated that nevertheless thrombosis plays but a minor rôle and that the primary aim should be drainage of the infected focus, *e g*, the lateral pharyngeal space which the pus reaches by lymphatics or direct extension from the nose and throat. According to him, ligation of the internal jugular vein is of secondary importance. It may be done if easily accessible, but is not absolutely necessary (Figs 2 to 7).

Space 4—This space, often referred to as the “danger space,” is the loose areolar space between the alar and prevertebral fasciae. It is limited laterally where these layers fuse at the tips of the transverse processes. It extends superiorly to the base of the skull and inferiorly into the posterior mediastinum. It is because of the latter relationship that it is often called the “danger space.” There was very little tendency for injected masses to spread beyond this space, the most common being into Space 4A. However, extension did occur from other spaces into this space, especially from Space 3. It is in this way that Ludwig’s infection and retropharyngeal abscesses find their way into the posterior mediastinum. As stated above, retropharyngeal abscess may start in Space 4 (by lymphatic extension from the nose and throat) or may secondarily extend into Space 4 from Space 3 (Figs 1 to 8).

Space 4A—This is the potential space between the superficial layer of deep fascia and the scalenus fascia. In the subclavian triangle, it lies between the sheath of the posterior belly of the omohyoid muscle and the scalenus fascia. This space is continuous with the axilla, but a rather dense fatty pad between the clavicle and first rib makes this communication less free (Figs 2 to 7).

Space 5—This is the potential space between the prevertebral fascia and the bodies of the vertebrae. It extends from the base of the skull to the coccyx and is limited laterally by the attachment of the prevertebral fascia to the transverse processes. There was very little tendency for injected masses to rupture through the walls of Space 5 into Spaces 4, 4A, and 5A. However, this did occur at times. Space 5 is the space involved in tuberculosis of the bodies of the vertebrae, resulting in cold abscesses. These usually extend inferiorly posterior to the prevertebral fascia along muscles taking origin from the vertebral bodies (psoas abscess). Sometimes they remain localized in the cervical region. They either stay posterior to the prevertebral fascia (in Space 5) or rupture through that layer and enter Space 4. However, the typical retropharyngeal abscess originates in the nose and throat and the typical cold abscess gravitates to a lower plane within Space 5 (Figs 1 to 8).

Space 5A—This space, posterior to the scalenus fascia, lies between the deep muscles of the back of the neck. Infections within it extend superiorly and inferiorly along these muscles, thus sometimes traveling great distances (Figs 2 and 4 to 8).

Suprahyoid Spaces. The Masticator, Temporal and Parotid Spaces—The *masticator* space is bounded by the superficial layer of deep fascia which, after forming the sheath of the masseter muscle, passes around the anterior and posterior borders of the ramus of the mandible and becomes continuous with the sheaths of the pterygoid muscles. The space thus contains the masseter muscle, the external and internal pterygoid muscles, and the ramus of the mandible. It is closed on all sides except superiorly, where it is in relation with the *temporal* space, deep to the deep temporal fascia. Injections into either space spread to the other, and under increased pressure, ruptured either superficially through the masseter sheath, or deeply into the parotid

space or lateral pharyngeal and submandibular spaces. The *parotid* space was found to be a completely closed space formed by a split of the superficial layer of deep fascia and occupied by the parotid gland, external carotid artery, and posterior facial vein. Injections made into this space showed infiltration into the substance of the gland and ruptures through the capsule superficially with subcutaneous collections and deeply with extensions into the masticator, lateral pharyngeal, and submandibular spaces (Figs 3, 4, 5 and 9).

The Lateral Pharyngeal Space—This important fascial space of the head is bounded by the pharynx, medially, the styloid muscles and carotid sheath, posteriorly, the parotid gland, posterolaterally, the mandible, pterygoids and masseter, anterolaterally, and the pterygomandibular raphe, anteriorly. Superiorly it extends to the base of the skull and inferiorly it is shut off from the neck by the attachment of the submaxillary capsule to the sheaths of the stylohyoid and the posterior belly of the digastric muscles. Inferomedially it communicates freely with the submandibular space deep to the submaxillary capsule. Posteromedially it communicates with Space 3. Injections made through the palatine tonsil and lateral pharyngeal wall went directly into the lateral pharyngeal space. From here, the injected masses spread easily into Space 3 and, in some cases, ruptured through the alar fascia into "danger space" 4. Extensions into the submandibular space took place freely. The lateral pharyngeal space is therefore infected from tonsillar abscesses, from retropharyngeal abscesses involving Space 3, and secondarily from the floor of the mouth through the submandibular space. Likewise, infections in this space may spread to the submandibular space and, in the later stages, resemble true Ludwig's angina (Figs 3, 4, 5 and 9).

The "Submandibular Space"—We have coined the term "submandibular space" to include the regions of the submental and submaxillary triangles lying between the mucous membrane of the floor of the mouth and the superficial layer of deep fascia over these regions. It thus encloses the sublingual and submaxillary salivary glands (the latter in a complete capsule), the genio-glossus, geniohyoid, mylohyoid and digastric (anterior belly) muscles. The floor or deep wall of this space is made up of the hyoglossus muscle and superior pharyngeal constrictor, the latter covered by visceral fascia. Thus a group of potential spaces, all communicating, is established between the submental muscles, crossing the midline and extending deep to the capsule of the submaxillary salivary gland, superolaterally, to become continuous with the lateral pharyngeal space. This group of spaces, collectively making up the submandibular space, is limited inferiorly at the hyoid bone where the submental muscles and their sheaths attach, and inferolaterally at the inferior borders of the stylohyoid and posterior belly of the digastric muscles, the sheaths which are attached to the superficial layer of deep fascia superficially and the carotid sheath deeply (Figs 3, 5 and 9).

Injections, made through the mucous membrane of the floor of the mouth, anywhere from the midline anteriorly to the anterior tonsillar pillar posteriorly

passed into the submandibular space. The more anterior injections first passed between the submental muscles and then spread laterally toward the lateral pharyngeal space deep to the submaxillary salivary gland. The more posterior injections passed into the lateral pharyngeal space more quickly. From the lateral pharyngeal space the injections often passed into Space 3, from where they sometimes spread to the superior mediastinum, or broke through the alar fascia and extended down Space 4 to the posterior mediastinum. This is the pathway taken by infection from the floor of the mouth in Ludwig's angina and is practically a reversal in direction of that taken by retropharyngeal abscess. The latter, therefore, by extension to the submandibular space, may resemble Ludwig's angina in the later stages, although the origin and early spread of the two conditions are entirely different (Figs 3, 5 and 9)

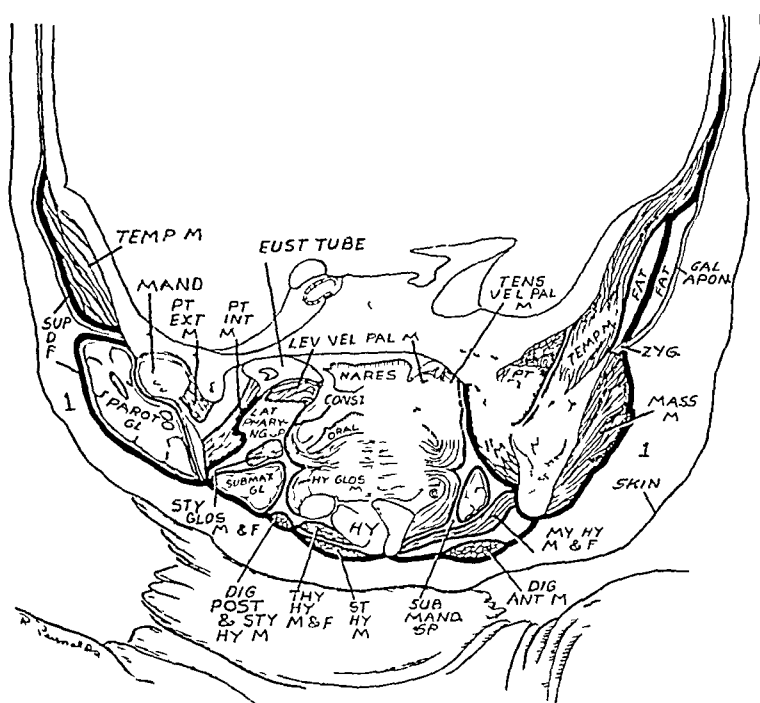


FIG 9—Frontal section of full term fetus through base of tongue and posterior nares. Anterior view

ETIOLOGY AND PATHWAYS OF SPREAD—Retropharyngeal abscess may be acute or chronic. The latter is usually due to tuberculous caries of the cervical vertebrae, is apt to be confined posterior to the prevertebral fascia in Space 5, and usually gravitates to lower levels along muscles taking origin from the vertebral bodies (psoas abscess). It is most common in adults (Fig 1).

The acute variety, on the other hand, is most common in children, especially under the age of three years. The portal of entry is practically always the nose, throat or middle ear. The infection passes through the pharyngeal wall by continuity or more commonly by lymphatics to the retropharyngeal and lateral pharyngeal nodes. Perhaps the greater number of retropharyngeal lymph nodes present under the age of three or four years accounts for the greater incidence in that age period (Morse, 1903, Meierhof, 1905, Alexander

and Montague, 1913) The possibility of spread through the veins from the pharynx to the internal jugular veins with thrombosis and secondary extension to the retro- and lateral pharyngeal spaces must also be kept in mind

Infection, extending through the lateral pharyngeal wall opposite the palatine tonsil either by direct continuity or by lymphatics, leads to direct infection of the lateral pharyngeal space On the other hand, infection from the posterior pharyngeal wall, nose (including the accessory sinuses) or middle ear may reach the retropharyngeal space by continuity or lymphatic extension As shown above, this infection may be in the visceral space, Space 3 or Space 4 As Space 3 and the lateral pharyngeal space are continuous, there may be extension from one to the other On the other hand, extension may occur from Space 3 to the superior mediastinum or through the alar fascia to Space 4 and thus to the posterior mediastinum It is because of the possibility of such extension that retropharyngeal and lateral pharyngeal abscesses are so serious (Figs 1 to 9)

The causative organisms are usually the common pyogens Koplik (1896) found the *Streptococcus* in all his cases The *Staphylococcus* and *pneumococcus* have also been reported as causative agents Bokay (Morse, 1903) reported a case due to the tubercle bacillus These organisms get into the retro- and lateral pharyngeal spaces by continuity, lymphatics or veins—either through inflammation of or trauma to (foreign bodies, operative trauma) the mucous membrane of the throat, pharynx, nose, accessory sinuses or middle ear

CLINICAL PICTURE *Acute Retropharyngeal Abscess*—The patient, as stated before, is usually a child (especially under three years), although adults are not immune (Allen, 1881, Goodale, 1901) The onset is usually sudden Following a nasopharyngitis, the patient develops chills and fever (103° to 105° F) There is usually stiffness of the neck muscles and the head may be in opisthotonos The throat is sore, the pain being aggravated by swallowing, which is difficult The voice assumes a nasal twang and thirst is marked Dyspnea and cyanosis occur as the swelling increases In young children, convulsions may ensue

On examination of the throat, a definite bulging of the posterior pharyngeal wall is noted This is usually a little to one side of the midline due to the fact that the retropharyngeal lymph nodes, which are usually involved, are distributed in two chains, one on either side of the midline (Morse, 1903, Meierhof, 1905, Waugh, 1906) Since such swellings are common without suppuration in ordinary lymphatic drainage from the nose, sinuses and nasopharynx, it is necessary to palpate the mass with the fingers to determine the presence of fluctuation and, in doubtful cases, even to needle the mass to prove the presence of pus Extension of the process to the superior or posterior mediastinum is indicated by chest pain, dyspnea, persistence or recurrence of fever and roentgenographic evidence of mediastinitis

Lateral Pharyngeal Abscess—This may be secondary to a retropharyngeal abscess, or abscess in the parotid, masticator, or submandibular (Ludwig's

angina) spaces, or it may be primary due to extension by continuity, lymphatics or veins from the tonsil, lateral wall of the pharynx, nose or middle ear. It may, therefore, be preceded or accompanied by symptoms of retropharyngeal abscess, parotitis or Ludwig's angina. On the other hand, the first localization may be in the lateral pharyngeal space, in which case there is sudden onset of severe pain and tenderness just below the angle of the jaw and over the greater cornu of the hyoid bone. There is considerable pain on swallowing and salivation is apt to be excessive. An external swelling below the angle of the jaw is usually apparent by the second or third day and, internally, there is a bulging of the lateral pharyngeal wall, especially posterior and inferior to the palatine tonsil. Chills and fever are usually present. However, chills do not necessarily mean thrombosis of veins unless they persist after adequate drainage of the space involved. The voice and respirations are not affected unless the swelling becomes very large or is associated with retropharyngeal abscess. It is obvious that in the later stages, retropharyngeal abscess, lateral pharyngeal abscess and Ludwig's angina may closely resemble each other, although the origin of each is quite different (Figs 3, 4, 5 and 9).

Chronic Retropharyngeal Abscess—As stated above, this is usually due to tuberculous caries of the cervical vertebrae and is, therefore, accompanied by other signs of that disease such as spinal deformity, spasm of the muscles of the back of the neck and associated cold abscesses gravitating to lower levels (psoas abscess). Roentgenographic evidence of caries of the cervical vertebrae confirms the diagnosis. Since the vertebral bodies are in the midline, this abscess is apt to cause forward bulging of the posterior wall of the pharynx in the midline, in contrast to the condition in acute retropharyngeal abscess (Figs 1 to 9).

TREATMENT—Early and adequate drainage is essential. There is some difference of opinion as to whether drainage should be internally through the posterior pharyngeal wall or externally through the neck. There are many reports of successful drainages through the mouth (Allin, 1851, Smith, 1879, Allen, 1881, Agnew, 1882, McCoy, 1882, Sands, 1882, de Blois, 1885, Tiely, 1891 and 1892, Moore, 1893, Beig, 1894, Wharton, 1894, Koplik, 1896, Evans, 1897, Goodale, 1901, Travers, 1902, Morse, 1903, Meierhof, 1905, Holmes, 1907, Sheedy, 1912, Alexander and Montague, 1913, McKenzie, 1915). The objections to this method are the danger of aspiration of pus into the lungs causing suffocation or secondary abscess, the possibility of secondary infection from the throat, and the tendency of internal incisions to close, making reoperation sometimes necessary. On the other hand, the simplicity of the procedure in comparison with the external approach favors its use. Furthermore, by quickly inverting the child after the incision, the danger of aspiration can be largely avoided (Figs 1, 3 and 5).

External drainage was first performed by Chiene (1877), who made an incision along the posterior border of the sternocleidomastoid muscle and reached the abscess by dissecting behind the carotid sheath. Similar operations were performed by Cheyne (1881), and Hawkins and Ambler (1889). On

the other hand, Buickhardt (1888) described and employed an approach anterior to the sternocleidomastoid muscle similar to the incisions described later by Dean (1919), Kanavel (1922) and Furstenberg (1929). Mosher (1929) advised external drainage through a "T" incision below the angle of the jaw in front of the sternocleidomastoid muscle, the submaxillary salivary gland being displaced and the dissection being carried along the carotid artery until the focus is reached. This incision is especially applicable to primary and secondary involvement of the lateral pharyngeal or pharyngomaxillary space. Dean's incision is made between the hyoid bone and the cricoid cartilage along the anterior border of the sternocleidomastoid muscle, and the dissection passes between the carotid sheath and the thyroid gland. This opens Space 3 and drains any collections in this space. By plunging through the alar fascia with the finger, Space 4 is entered, and collections deeper in the retropharyngeal space and posterior mediastinum are drained. By going still deeper, through the prevertebral fasciae, Space 5 collections (due to caries of the vertebrae) may be also drained through this approach. Furstenberg's incision for cervical mediastinotomy is similarly placed but extends inferiorly to the suprasternal notch (Figs 2, 6 and 7).

It seems logical to drain small localized acute retropharyngeal abscesses without external swelling through the mouth, with proper precautions to prevent aspiration into the lungs. On the other hand, lateral pharyngeal collections, whether primary or secondary, with tumefaction externally at the angle of the jaw, are best drained by Mosher's or similar external approach. This will probably also take care of any associated retropharyngeal abscess. Cold abscesses should certainly be drained externally by the method of Dean in order to prevent secondary infection from the throat. Such incisions may even be closed tight after evacuating the pus (Kanavel, 1929).

Mediastinotomy is indicated at the first sign of spread beyond the retro- or lateral pharyngeal spaces toward the superior or posterior mediastinum. There are in general two methods of approach. The collar (cervical) mediastinotomy of Luimann (1876), Obalinski (1896), Cavazzani (1898), Ziembecki (1898), Heidenham (1899), Rasumowski (1900), von Hacker (1901), Guadiani (1916), Lerche (1921 and 1924), and Furstenberg (1929), and the dorsal (thoracic) mediastinotomy, first described by Nasiloff (1888). The collar drainage has already been described according to the technic of Dean and Furstenberg. This method is especially applicable to collections in the superior mediastinum (Space 3) and in the posterior mediastinum (Space 4) above the fourth thoracic vertebra (Figs 2, 6 and 7). Dorsal mediastinotomy is especially indicated in collections in the posterior mediastinum below the fourth thoracic vertebra and as a secondary operation after collar mediastinotomy (Fig 8). Various technics of dorsal mediastinotomy have been described by Quenu and Hartmann (1891), Bryant (1895), Heidenham (1899), Enderlen (1901), and Lilienthal (1923). These vary chiefly in the location of the incision in relation to the vertebral spines. The reader is referred to these authors for details and procedure.

CASE REPORTS

Case 1—University Hospital No 42968 D F, male, age 15 months, entered the University Hospital complaining of sore throat and difficulty in swallowing. Two weeks previously, he had contracted an acute respiratory infection and the cervical lymph nodes became enlarged. External cold packs were applied and seemed to localize the infection on the inside, behind the pharyngeal wall. Examination showed an infant of stated age with temperature of 101° F, pulse 150, respirations 32, apparently in considerable discomfort. The throat showed a bulging of the posterior pharyngeal wall a little to the right of the midline. Definite fluctuation could be appreciated upon digital examination. *Diagnosis* Retropharyngeal abscess resulting from adenitis and paradenitis of the retropharyngeal lymph nodes, which in turn were infected from the nose and nasopharynx.

Treatment—The abscess was incised through the posterior pharyngeal wall and the wound spread with a hemostat, according to the method of Hilton, on the day of entrance. Considerable thick, yellow pus was obtained which was permitted to drain out, with the child's head lowered to prevent aspiration. Uneventful convalescence. Patient was dismissed five days after entrance to the hospital.

COMMENT—This is a case of typical retropharyngeal abscess secondary to adenitis and paradenitis of the retropharyngeal lymph nodes, following lymphatic extension from the nasopharynx. The retropharyngeal abscess probably occupied Space 3, and was also localized by an inflammatory wall. There was, therefore, very little tendency to extend laterally and inferiorly, and this probably explains the good results from simple internal drainage.

Case 2—University Hospital No 23976 N F, female, age seven months, was brought to the University Hospital because of difficulty in breathing. She had been well until about seven weeks previous to entrance, when she contracted a sore throat and later a discharging ear. The posterior cervical nodes became enlarged, and were later incised. During the week previous to entrance, the parents noticed difficulty in her breathing, which had become worse during the last 24 hours. The patient had lost six pounds during this period. Examination showed a very pale, emaciated child with a temperature of 101° F. She was breathing with marked difficulty. The cervical nodes were enlarged, a soft, fluctuating group being present on the right. The posterior pharyngeal wall, a little to the right of the midline, was bulging, and fluctuated. *Diagnosis* Retropharyngeal abscess. Suppurating cervical lymph nodes.

Treatment—An internal incision through the posterior pharyngeal wall was made without anesthesia. Several ounces of thick pus were evacuated and the patient's head was lowered to prevent aspiration. The fluctuating cervical nodes were incised and drained. The child improved gradually and was dismissed from the hospital three weeks after operation.

COMMENT—This presents another case of retropharyngeal abscess in an infant involving chiefly Space 3, and localizing in the posterior pharyngeal region. There was also primary and secondary lymphatic drainage from the nasopharynx to the pendent group of lymph nodes which suppurated and required separate incision.

Case 3—University Hospital No 51689 W H, male, age two months, was brought to the University Hospital because of difficulty in breathing, of about six hours duration. The baby had been poorly nourished since birth, but had had no serious illness until one week before entrance, when a rounded swelling the size of a cherry was first noticed on the left side, a little below and posterior to the angle of the jaw. The swelling had increased considerably. About six hours before entrance, the baby had developed difficulty in

breathing, which had become progressively worse. Examination showed a poorly nourished child apparently in severe distress. Temperature, 100° F. There was a marked nasal and postnasal discharge. The cervical nodes were enlarged, with a large, hard swelling below the angle of the jaw on the left. The posterior pharyngeal wall was bulging, especially a little to the left of the midline. This swelling fluctuated. Both ear drums were dull, thick and red. *Diagnosis* Postnasal discharge. Bilateral otitis media. Cervical adenitis. Retropharyngeal abscess.

Treatment—The retropharyngeal abscess was incised through the mouth, with evacuation of thick pus. The head was lowered to prevent aspiration. A double paracentesis was performed, a bilateral mastoidectomy was, however, necessary a week later.

Postoperative Course—The baby apparently recovered from the retropharyngeal abscess and mastoid operations, but died two weeks after entrance from malnutrition.

COMMENT—The retropharyngeal abscess in this case may have been due to lymphatic drainage from either the nasopharynx or middle ear. Drainage of the retropharyngeal abscess and ears was apparently early and adequate, but the child succumbed because of malnutrition.

Case 4—University Hospital No 42267 D B, male, age 33, entered the University Hospital complaining of sore throat and difficulty in swallowing. About two weeks previously he had developed the "flu" and sore throat. About five days before admission, his throat had become very sore and he was not able to swallow or talk. He was unable to sleep because of pain on involuntary swallowing, and was unable to take fluids or food. Examination showed a very emaciated young man, unable to swallow or talk above a whisper. Temperature was 100° F, pulse 60, respirations 18. Local examination revealed a large, red swelling of the posterior pharyngeal wall, pushing the tonsils forward and pressing against the uvula. *Diagnosis* Retropharyngeal abscess.

Progress—The abscess ruptured spontaneously and the patient made an uneventful recovery without surgery.

COMMENT—This is a case of retropharyngeal abscess in the adult. Although it is possible that the infection passed directly through the posterior pharyngeal wall, it is more likely that the extension was by the lymphatics which, though less abundant than in early childhood, are still present in the adult. The abscess was no doubt localized in Space 3, thus making the spontaneous rupture possible.

Case 5—University Hospital No 57412 M G, female, age 63, entered the University Hospital complaining of pain and fullness in the neck at the level of the cricoid cartilage. The night before, while eating supper, she had a sudden severe pain in her throat which later moved to the epigastrium and was referred to the back. Laryngoscopic examination was negative and esophagoscopy revealed only a red, edematous mucosa. Roentgenologic examination of the esophagus was negative and study of the chest revealed accentuation of the vascular markings with an area of calcification lateral to the right hilum. Soon after entrance, she experienced considerable difficulty in swallowing. Two days later she became suddenly cyanotic and expired. Autopsy revealed a retropharyngeal abscess and posterior mediastinitis.

COMMENT—This case is a good example of retropharyngeal abscess involving Space 4, due to trauma of the pharyngeal wall rather than to lymphatic spread from the ear, nose or throat. There was very little tendency to localize in the head and cervical region (by inflammatory reaction) but, instead, the abscess gravitated to the posterior mediastinum which is directly

continuous with Space 4. The mediastinitis was not recognized antemortem. Possibly if it had been, and drainage had been instituted, the fatal outcome might have been averted.

Case 6—University Hospital No 41614 C A, male, age seven, was admitted to the University Hospital with a history of having swallowed a tack one week previously. The tack was recovered in his stool six days later. His throat became very sore, he was unable to swallow, and his voice became nasal in type. Examination showed a thin, poorly nourished boy having some difficulty in breathing, swallowing and talking. The throat was red. The posterior cervical lymph nodes were palpable and the anterior neck was swollen from the mastoid to the submaxillary regions. Roentgenologic examination showed encysted fluid or pus behind the posterior pharyngeal wall at the level of the glottis. Examination of the throat showed a bulging of the posterior pharyngeal wall which compressed the epiglottis, and interfered with respiration and deglutition. *Diagnosis* Retropharyngeal abscess following trauma.

Treatment—On the eve of entrance, the child suddenly became cyanotic and more dyspneic, making a tracheotomy necessary. A little gas escaped from the sides of the larynx and trachea. Following this, the posterior pharyngeal wall was incised through the mouth and about two ounces of thick, yellow pus escaped. Patient made an uneventful convalescence and was discharged six days after entrance.

COMMENT—This is another example of retropharyngeal abscess due to trauma of the posterior pharyngeal wall. In this case, however, the tack apparently penetrated only the pharyngeal wall and visceral fascia, thus infecting Space 3. There was some inferior and lateral extension in Space 3, but most of the infection remained localized in the oral region and was successfully drained through the mouth after a preliminary tracheotomy which included drainage of Space 3 on either side of the trachea and esophagus.

Case 7—University Hospital No 18600 C S, male, age 28, entered the University Hospital complaining of pain in his throat, difficulty in swallowing, and pain in the neck. While eating dinner three days previously, he had experienced a sudden pain in his throat as though the bolus were lodged there. Since then there had been severe pain, especially on trying to swallow, and he had been unable to take anything except liquids. Twenty-four hours before entrance to the hospital, his neck had become swollen and tender. Examination showed the neck tense, red, and tender from the thyroid cartilage to the sternum. The throat was red. Roentgenologic examination showed a shadow of a foreign body anterior to the sixth cervical vertebra, possibly at the entrance of the esophagus. A directoscope was passed and a large bone was removed from the esophageal wall. The temperature on entrance was 102.4° F, pulse 104. *Diagnosis* Foreign body Retropharyngeal abscess extending through the neck to the superior mediastinum.

Subsequent Course and Treatment—Patient carried a septic temperature (101 to 104.2° F), rapid pulse (120 to 140), and rapid respirations (32 to 45). He had considerable difficulty in breathing. On the third day the neck was incised anterior to the left sternocleidomastoid muscle and considerable pus evacuated from around the thyroid gland and esophagus (Space 3). At this time the blood culture was positive for Staphylococcus and Streptococcus. The patient continued to run a septic temperature and in spite of supportive measures died rather suddenly.

Autopsy revealed a retropharyngeal abscess (traumatic), fascial space abscess of the neck (Space 3) and superior mediastinitis.

COMMENT—Again we see a case of retropharyngeal abscess in Space 3, due to trauma of the pharyngeal wall. In this case, the foreign body entered

rather low (at the junction of the pharynx and esophagus, about the level of the sixth cervical vertebra) and the infection passed laterally and inferiorly, finally reaching the superior mediastinum. Cervical mediastinotomy was performed perhaps a little late, but the septicemia present would probably have led to fatal outcome even with earlier surgical intervention.

Case 8—University Hospital No 20411. A. H., female, age 34, entered the University Hospital complaining of sore throat, inability to swallow, and pain in the left ear. Two weeks previously, she had taken cold, her throat had become sore, and she had developed an earache. A few days before entrance, her neck had become swollen on the outside. Examination showed an obese woman, apparently in severe pain. There was a swelling on the left side of the neck extending from the ear almost to the clavicle. It was hard and indurated. The throat was red and there was a definite bulging of the lateral pharyngeal wall on the left side. There was a small amount of pus coming from an opening just above the tonsil. Temperature 103.5° F, pulse 130. *Diagnosis*: Lateral pharyngeal abscess.

Treatment—The day after admission, an incision was made anterior to the left sternocleidomastoid muscle and a small amount of thick pus was obtained. The temperature remained high (106° F), pulse rapid and respirations difficult. The patient gradually became weaker and expired two days after admission. No autopsy.

COMMENT—This case is an example of lateral pharyngeal abscess resulting from direct extension through the lateral pharyngeal wall or lymphatic extension from the throat or middle ear. Extension through the venous system is also a possibility. Unfortunately no autopsy was obtained, but the clinical course suggests that the infection extended from the lateral pharyngeal space to Space 3 by continuity. From Space 3 the infection, no doubt, spread inferiorly through the neck to the superior mediastinum. It is also likely that the abscess ruptured through the alar fascia to enter Space 4, and extended inferiorly into the posterior mediastinum. The cervical incision was obviously inadequate to properly drain the spaces involved.

Case 9—University Hospital No 175. H. H., male, age 32, entered the University Hospital complaining of sore throat, swelling of the neck, pain in the chest, dyspnea, chills, and fever. About two weeks before entrance, patient had "La grippe" accompanied by sore throat. About one week later, his neck began to swell, and he experienced difficulty in swallowing and talking. A few days before entrance, he had had a severe chill lasting an hour. This was followed by pain in the center of the chest and difficulty in breathing, symptoms which were present on entrance. Examination showed a very ill man. Temperature 104.4° F, pulse 124, respirations 36. The throat was red but not bulging. The neck was swollen and indurated on both sides from the mandible to the sternum and clavicles. Dulness and moist râles were present over the lower right lobe of the lung. *Diagnosis*: Deep neck abscess and right empyema.

Subsequent Course and Treatment—Three days after entrance, the neck was drained by bilateral incisions and much pus obtained. The next day, a right empyema was drained through an intercostal incision. Patient did poorly and died the following morning.

Autopsy—Infection of the deep spaces of the neck secondary to retropharyngeal abscess and leading to posterior mediastinitis. Secondary right empyema by extension of infection from the posterior mediastinum.

COMMENT—This patient no doubt had a severe nasopharyngitis during his attack of “La grippe” two weeks before entrance. The infection then spread by the lymphatics to the retropharyngeal nodes, causing an adenitis and paradenitis of these nodes, and resulting in a retropharyngeal abscess. The latter, however, did not remain localized in the retropharyngeal space (therefore, there was no bulging of the posterior pharyngeal wall), but extended inferiorly in Space 4, producing a posterior mediastinitis. The swelling in the neck was no doubt due to accumulation of pus in Space 4, but there may also have been some inferior extension in Space 3, and an adenitis of the pendent group of lymph nodes by drainage from the nose and throat. The incisions in the neck were late and inadequate, and no attempt was made to drain the mediastinum, although the secondary empyema on the right side was drained. It is conceivable that earlier and more adequate drainage might have resulted in a different outcome. This, in turn, would have required an earlier and more complete diagnosis based upon anatomic grounds.

CONCLUSIONS

(1) Acute retropharyngeal and lateral pharyngeal abscesses are secondary to infection of the nose, throat or middle ear. They are more common in young children under the age of three years. This may be due to the greater abundance of lymphatics in that age-period. The common pyogens are usually the responsible organisms.

(2) The infection reaches these spaces by direct continuity, venous or lymphatic drainage, the latter being most common except where trauma is a factor, in which case the spread is by direct implantation.

(3) Acute retropharyngeal abscess may involve the space between the pharyngeal wall and the visceral fascia (visceral space), the space between the visceral and alar fasciae (Space 3) or the space between the alar and prevertebral fasciae (Space 4).

(4) Infection in the visceral space is apt to remain localized at the site of origin. Infection in Space 3 may remain localized at the site of origin, but may also spread inferiorly and laterally through the neck to the superior mediastinum. It may also break through the alar fascia and reach Space 4. Infection in Space 4 (“danger space”) is apt to gravitate through the neck into the posterior mediastinum.

(5) The lateral pharyngeal space is directly continuous with Space 3. It may be primarily infected from the lateral pharyngeal wall or may be secondarily infected from Space 3, the parotid space, masticator space or submandibular space. Vice versa, primary infection within the lateral pharyngeal space may spread secondarily into those spaces. Infection in the lateral pharyngeal space extending into the submandibular space may resemble Ludwig’s angina in the later stages.

(6) Chronic retropharyngeal abscess is practically always due to tuberculous caries of the cervical vertebrae. It is usually confined to Space 5 behind

the prevertebral fascia, and usually gravitates to lower levels along muscles taking origin from the vertebral column (psoas abscess). It may, however, remain localized in the cervical region, in which case it may rupture through the alar fascia and enter "danger space" 4. It is more common in adults.

(7) The clinical picture of pain, difficulty in swallowing and speaking, chills and fever, internal bulging of the pharyngeal wall, and external swelling of the neck should make early diagnosis possible.

(8) The treatment is chiefly surgical—early and adequate drainage. This may be internal through the mouth for cases confined to the posterior pharyngeal region (visceral space and Space 3). External incision is necessary for collections in the lateral pharyngeal space or inferior extensions in Spaces 3 or 4. The "T" incision of Mosher with reflection of the submaxillary salivary gland is especially applicable for collections in the lateral pharyngeal space. Spaces 3 and 4, including collections in the superior mediastinum and posterior mediastinum above the fourth thoracic vertebra, may be effectively drained by cervical incision anterior to the sternocleidomastoid muscle (collar mediastinotomy). Collections in the posterior mediastinum below the level of the fourth thoracic vertebra demand posterior thoracic drainage (dorsal mediastinotomy).

NOTE.—The illustrations are reproduced through the courtesy of the *American Journal of Anatomy*.

BIBLIOGRAPHY

- ¹ Adams, W. T. Retropharyngeal Abscess in Infants with Report of Cases. *Northwest Lancet*, 23, 93, 1903.
- ² Agnew, D. H. Abscess of the Pharynx. *Med and Surg Reporter*, 47, 65, 1882.
- ³ Alexander, I. H., and Montague, H. Acute Retropharyngeal Abscess. *N. Y. Med J.*, 98, 227-229, 1913.
- ⁴ Allen, H. Case of Retropharyngeal Abscess in the Adult. *Arch Laryng*, 2, 46-49, 1881.
- ⁵ Allin, C. M. Retropharyngeal Abscess. *N. Y. Med J.*, 7, 307-342, 1851.
- ⁶ Badgerow, G. W. Pharyngeal Suppuration, Course and Direction of Various Types. *Lancet*, 1, 780-782, 1912.
- ⁷ Ball, F. E. Acute Suppurative Mediastinitis. *Arch Otolaryng*, 4, 512-514, 1926.
- ⁸ Barnhill, J. F. Surgical Anatomy of the Head and Neck. Wm. Wood & Co., Baltimore, 1937.
- ⁹ Beck, A. L. A Study of Twenty-four Cases of Neck Infection. *Tr. Am. Acad. Ophthalmol. and Otolaryng.*, 37, 342-381, 1932.
- ¹⁰ Beck, C. Suppurative Mediastinitis Following a Retropharyngeal Abscess, Drainage, Recovery. *North Amer. Pract.*, 6, 255-259, 1894.
- ¹¹ Berg, H. W. Causation, Pathology and Symptoms of Retropharyngeal Abscess. *Med. Rec.*, 45, 522-524, 1894.
- ¹² Blair, A. M. The Differential Diagnosis of Mediastinal Conditions. *Am. J. Med. Sci.*, 154, 240-251, 1917.
- ¹³ Bryan, W. A. Mediastinal Abscess. *J. Tennessee Med. Assn.*, 14, 405, 1922.
- ¹⁴ Bryant, J. D. Surgical Technique of Entry to the Posterior Mediastinum. *Tr. Am. Surg. Assn.*, 13, 443-459, 1895.
- ¹⁵ Burckhardt, H. Über die Eröffnung der retropharyngealen Abscess. *Centralbl. f. Chir.*, 15, 57-59, 1888.

- ¹⁶ Cavazzani Ascesso del mediastino posteriore diagnosticato e operato con toracotomia dorsale *Riforma Medica*, 1898
- ¹⁷ Cheyne, W W Case of Retropharyngeal Abscess Pointing in the Pharynx, but Opened by an Incision Behind the Sternocleidomastoid, Cure *Med Times and Gaz*, 2, 254, 1881
- ¹⁸ Chiene, J Retropharyngeal Abscess *Brit Med J*, 2, 255, 1877
- ¹⁹ Clutton, H Retropharyngeal Abscess *Brit Med J*, 1, 395, 1887
- ²⁰ Cook, O S Acute Mediastinal Abscess *Am J Roent*, 10, 696-698, 1923
- ²¹ Cooper, H An Unusual Pharyngeal Abscess *Brit Med J*, 2, 291, 1933
- ²² Davidson Postpharyngeal Abscess, Asphyxia, Laryngotomy, Recovery *Lancet*, 2, 881, 1892
- ²³ de Blois, T A Two Cases of Retropharyngeal Abscess *Boston Med and Surg Jour*, 113, 53-54, 1885
- ²⁴ Dean, L W The Proper Procedure for External Drainage of Retropharyngeal Abscess Secondary to Caries of the Vertebrae *Ann Otol, Rhin and Laryng*, 28, 566-572, 1919
- ²⁵ Enderlen Ein Beitrag zur Chirurgie des hinteren Mediastinum *Deutsch Ztschr f Chir*, 61, 441-495, 1901
- ²⁶ Elliot, C Retropharyngeal Abscess *Brit Med J*, 1, 663, 1879
- ²⁷ Evans, T C Postpharyngeal Abscess *Pediatrics*, 4, 346-351, 1897
- ²⁸ Fulkerson, C B Report of a Case of "Otogenic Pharyngeal Abscess" with Review of Literature *J Michigan Med Soc*, 15, 301-304, 1916
- ²⁹ Furstenberg, A C Acute Mediastinal Suppuration *Tr Am Laryng, Rhin and Otol Soc*, 35, 210-229, 1929
- ³⁰ Furstenberg, A C Acute Suppuration of Throat, Mouth and Cervical Region *Trans Pac Coast Oto-ophth Soc*, 21, 14-25, 1936
- ³¹ Goldstein, M A Retropharyngeal Abscess Report of Some Unusual Cases *Tr Am Acad Ophth and Otolaryng*, 155-165, 1907
- ³² Goodale, J L Retropharyngeal Abscess in the Adult *Boston Med and Surg J*, 144, 108, 1901
- ³³ Grodinsky, M, and Holyoke, E The Fasciae and Fascial Spaces of the Head, Neck and Adjacent Regions *Am J Anat*, 63, 367-408, 1938
- ³⁴ Grodinsky, M Ludwig's Angina An Anatomical and Clinical Study with Review of the Literature Accepted for publication in *Surgery*
- ³⁵ Guadiani, V The Surgical Treatment of Suppuration in the Posterior Mediastinum *ANNALS OF SURGERY*, 63, 523-532, 1916
- ³⁶ Heidenhain, L Uber einen Fall von Mediastinitis suppurativa postica *Arch f klin Chir*, 59, 199-205, 1899
- ³⁷ Harper, J Acute Phlegmon of the Pharynx, with Some Notes on a Recent Case *Practitioner*, 86, 577-581, 1911
- ³⁸ Hawkins-Ambler, G A Retropharyngeal Abscess *Brit Med J*, 2, 644, 1891
- ³⁹ Holmes, E M Middle Ear Suppuration as an Etiologic Factor in Retropharyngeal Abscess *Tr Am Laryng, Rhin and Otol Soc*, 12, 24-45, 1907
- ⁴⁰ Horner Anomalous Case *Am Med Rec*, 1, 22-29, 1818
- ⁴¹ Kanavel, A B Retropharyngeal Abscesses *Surg Clin North Amer*, 2, 603-615, 1922
- ⁴² Kirschner Ein neues Verfahren der Oesophagoplastik *Arch f klin Chir*, 114, 606-663, 1920
- ⁴³ Koplik, H The Acute Retropharyngeal Abscess in Childhood *N Y Med J*, 63, 440-445, 1896
- ⁴⁴ Lambert, A V S, and Berry, F B Paths of Extension of Infection from Focus in Mediastinum *Arch Surg*, 14, 261-284, 1927
- ⁴⁵ Lerche, W Surgical Treatment of Suppuration in Posterior Mediastinum *Surg, Gynec and Obstet*, 32, 232-234, 1921

- ⁴⁶ Leiche, W Suppuration in the Posterior Mediastinum with Report of Cases Arch Surg, 8, 247-264, 1924
- ⁴⁷ Levy, W Versuche uber die Resection der Speiserohre Arch f klin Chir, 56, 839-892, 1898
- ⁴⁸ Lilienthal, H Posterior Mediastinotomy Arch Surg, 6, 274-284, 1923
- ⁴⁹ Lurmann Ein Fall von Oesophagus-fistel mit secundarer Bildung eines mediastinal Abscesses Berl klin Wchnschr, 9, 1876
- ⁵⁰ McCoy, A W Idiopathic Retropharyngeal Abscess Med and Surg Reporter, 46, 313, 1882
- ⁵¹ McGinnis, E Mediastinitis as Occasional Resultant Complication of Foreign Bodies in Esophagus Laryngoscope, 34, 831-835, 1924
- ⁵² McKenzie, D Otogenic Pharyngeal Abscess J Laryng, 30, 12-29, 1915
- ⁵³ Meierhof, E L A Safe and Adequate Method for Opening Retropharyngeal Abscesses in Children Laryngoscope, 15, 467-471, 1905
- ⁵⁴ Moore, J W Retropharyngeal Abscess Tr Roy Acad Med Ireland, 2, 60-63, 1892-1893
- ⁵⁵ Morse, J L Retropharyngeal Abscess in Infancy J A M A, 40, 281-284, 1903
- ⁵⁶ Mosher, H P Deep Cervical Abscess and Thrombosis of the Internal Jugular Vein Laryngoscope, 30, 365-375, 1920
- ⁵⁷ Mosher, H P The Submaxillary Fossa Approach to Deep Pus in the Neck Tr Am Acad Ophth and Otolaryng, 34, 19-36, 1929
- ⁵⁸ Myer, W Incision of Retropharyngeal Abscess According to Antiseptic Principles, From the Neck Am Med and Surg Bull, 9, 454-457, 1896
- ⁵⁹ Nasiloff, J J Oesophagotomia et resectio oesophagi endothoracica Vrach 9, 481, 1888
- ⁶⁰ Obalinski Beitrag zur operativen Behandlung des hinteren Brustfelbraumes Wien klin Wchnschr, 1896
- ⁶¹ Palmer, F E Pharyngomaxillary Abscess Colorado Med, 30, 79-81, 1933
- ⁶² Parker, F L Abscess of Tonsils, Pharynx and Tongue Med News, 43, 119-122, 1883
- ⁶³ Pearse, H E Mediastinitis Following Cervical Suppuration ANNALS OF SURGERY, 108, 588-611, 1938
- ⁶⁴ Porter, C T Unrecognized Complications Secondary to Peritonsillar and Lateral Pharyngeal Abscess, with Case Reports Arch Otolaryng, 26, 127-131, 1937
- ⁶⁵ Pretty, W Case of Gangrenous Inflammation in the Neck Med Times and Gaz, 17, 5-7, 1858
- ⁶⁶ Quenu et Hartmann Des voies de pénétration chirurgicale dans le mediastin posterieur Bull et Mem, Soc de Chir de Paris, 17, 82-85, 1891
- ⁶⁷ Rasumowski In Hildebrandt's Jahresbericht, p 411, 1900
- ⁶⁸ Rehn, E Operation an dem Brustabschnitt der Speiserohre Arch f klin Chir, 57, 733-755, 1898
- ⁶⁹ Richardson, C W Acute Abscess of the Lateral Wall of the Laryngopharynx Ann Otol, Rhin and Laryng, 29, 804-805, 1920
- ⁷⁰ Salinger, S, and Pearlman, S J Hemorrhage from Pharyngeal and Peritonsillar Abscesses Arch Otolaryng, 18, 464-509, 1933
- ⁷¹ Sands, H B Posterior Pharyngeal Abscess Med Rec, 22, 106, 1882
- ⁷² Savoy, W S A Case of Abscess in the Neck Lancet, 2, 696, 1880
- ⁷³ Sheedy, B Pharyngeal Abscess Med Rec, 81, 1226-1228, 1912
- ⁷⁴ Smith, E N Retropharyngeal Abscess Brit Med J, 1, 736, 1879
- ⁷⁵ Taylor, J Case of Laryngitis, Pharyngeal Abscess Extending Throughout the Posterior Mediastinum from Pharynx to Diaphragm Lancet, 1, 74-77, 1846
- ⁷⁶ Tieley, H E Retropharyngeal Abscess, Necessitating Intubation, Recovery Omaha Clinic, 4, 81-82, 1891-1892
- ⁷⁷ Travers, F T Retropharyngeal Abscess, Secondary Hemorrhage Brit Med J, 2, 703-704, 1902

- ⁷⁸ Tyler, L Retropharyngeal Abscess Med Rec , 22, 273, 1882
- ⁷⁹ Von Hacker Zur operativen Behandlung der perioesophagealen und mediastinalen Phlegmone nebst Bemerkungen der collaren und dosalen Mediastinotomie Arch f klin Chir , 64, 479-508, 1901
- ⁸⁰ Waldapfel, R Posttonsillitis Pyemia Tr Am Acad Ophth and Otolaryng , 33, 291-296, 1928
- ⁸¹ Wagner, L C Posterior Mediastinal Abscess Following Suppurative Arthritis of Cervical Vertebrae ANNALS OF SURGERY, 87, 511-516, 1928
- ⁸² Waugh, G E A Lecture on Pharyngeal Abscesses Lancet, 2, 845-846, 1906
- ⁸³ Wharton, H R Retropharyngeal Abscess Internat Clinics, 2, 197-199, 1894
- ⁸⁴ Ziembiecki Du Phlegmon du mediastin posterieur, 1895 Ref in Potarca La Chir , etc , Paris, 1898

PRIMARY LYMPHOSARCOMA OF THE STOMACH

EARL S TAYLOR, M D

NEW YORK

FROM THE SURGICAL SERVICE OF THE PRESBYTERIAN HOSPITAL AND THE SURGICAL PATHOLOGICAL LABORATORY COLLEGE
OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK, N Y

PRIMARY lymphosarcoma of the stomach is not a common surgical disease. They comprise from 40 to 50 per cent of all gastric sarcomata, which, in themselves, form but 1 to 2 per cent of all gastric neoplasms. However, with the increase of surgical procedures upon the stomach, it was felt of value to consider these lesions from a diagnostic and prognostic point of view, especially as it is improbable that any one surgeon will deal with any large number of cases, whereby he may judge the value of a particular type of therapy.

No attempt will be made to clarify the perplexing problem of neoplastic and neoplastic-like lesions of the lymphoid system. Until a clearer conception of the histogenesis of these lesions is available, disagreement in both terminology and classification is inevitable. An effort has been made here to include only those cases of lymphosarcoma that arise primarily from the lymphoid tissue of the stomach and are not a part of like changes taking place simultaneously in similar tissue in other portions of the body. Cases with insufficient data and those that were not clear-cut histologically have been omitted from the statistics. However, for the sake of completeness, a number of these closely related cases¹ have been included in the bibliography.

Five proven cases were found in the files of Presbyterian Hospital. These will be reported in detail, as they seem significant in calling attention to variations in the natural history of the disease—particularly in viewing the outcome in relation to the treatment given.

In 1871, Cruveilhier reported the first case of gastric lymphosarcoma (quoted from Forni). By 1914, Forni, in collecting 200 cases of gastric sarcoma, found 33 lymphosarcomata. He, for the first time, emphasized the necessity of a histopathologic classification of these sarcomata, to supplant the purely morphologic, endogastric and exogastric, division. D'Aunoy and Zoeller, in 1929, reviewed the literature and brought Forni's series up to date. Since then, except for case reports and small series from individual clinics, there has been no extensive review of the literature. The data presented here will be based on 152 cases of primary lymphosarcoma collected from the literature up to 1937, including five cases reported for the first[†] time from this hospital.

Etiology—The average age of the patients in this series was 44.3 years, which closely approximates the figures quoted by most authors. The youngest

Submitted for publication July 8, 1938.

* References for these cases are marked with an asterisk in the bibliography.

† Case 5 was presented, in 1933, by Dr. David Bull before a meeting of the New York Surgical Society.

case was three years and eight months old. He recovered after subtotal resection. The oldest patient was 80 years of age, on whom the diagnosis was made at postmortem. It will be seen that the average age of these patients is about 10 years younger than of those with carcinoma. Furthermore, there is a considerably greater proportion in the first four decades of life than would be found in a similar carcinoma series, 20 of 114 cases being less than 40 years of age.

The sex is known in 124 cases. There are 78 males and 46 females, a ratio of 1.6 to 1—a less marked male preponderance than the 3 to 1 usually quoted for carcinoma.

As with most neoplasms, there has been considerable speculation regarding the etiology of these tumors. Perhaps the most prominent "exciting cause" has been attributed to trauma. This causative factor was made much of by many of the early authors. However, although there are striking examples of coincidental injuries preceding discovery of the lesion, critical examination of the data is far from conclusive.

Peptic ulcer also has been incriminated as a precursor of these tumors. No such relationship has been borne out on histologic examination, even though the gross appearance at operation is very suggestive of gastric ulcer.

Although it has often been suggested that benign lesions of the stomach may degenerate into malignant ones—polyps to carcinoma or myoma to sarcoma—there is no evidence that lymphosarcoma arises from such growths.

Some pathologists feel that tuberculous lesions of the stomach may be the irritative and initiating factor—particularly in the presence of aberrant, undifferentiated cells in the submucosa.

Pathology—Primary lymphosarcoma of the stomach can arise from any lymphatic tissue in the organ. It is probable, however, that the lesion begins most often in a lymph follicle in the submucosa. From this point of origin, it penetrates along the tissue spaces and infiltrates the various layers. The muscle layers particularly are involved, each band of muscle being separated by large masses of tumor cells. The submucosa is enormously thickened, and this explains the giant rugae that are sometimes seen in a roentgenogram. The mucosa, not being the site of the original growth, does not show the early characteristic ulceration of carcinoma. However, later ulceration does take place, and "characteristic" ulcer niches and craters may develop. These tend to be more shallow than in carcinoma and frequently are multiple. Involvement of the serosa is usually a late manifestation but often assumes great proportions. Due perhaps to compromise of the blood supply by diffuse infiltration of all the layers, necrosis is frequent, and for this reason perforation is not uncommon.

Grossly, the lesions may be divided into four types (Pack and McNeer, 1935): (I) A single bulky polypoid growth well demarcated from the normal stomach, (II) solitary or multiple ulcers with surrounding infiltration, (III) multiple nodular tumors in the submucosa, (IV) diffuse thickening of the wall. This last type strongly resembles the fibrocarcinoma designated as

"*limitis plastica*"—except that the stomach is not contracted and large mucosal folds are frequently present. Unfortunately, the largest number are of Types II and IV. As the well demarcated growths are comparatively infrequent, lymphosarcoma does not share the advantages that some other of the sarcomas have over carcinoma from a surgical standpoint. The large pedunculated growths of the exogastric type found in other types of sarcoma are not found with lymphosarcoma.

Gross diagnosis is not always possible. The lesion is most frequently confused with carcinoma. Some cases have been treated operatively on the assumption that a peptic ulcer was the basis of the pathology. Gastric syphilis may also be confusing, but the frequent presence of large, isolated, succulent perigastric nodes may serve to differentiate this condition.

The curvatures are usually considered as being the commonest site of origin. Actual involvement of the orifices is unusual, although the lesions frequently extend to involve both the anterior and the posterior walls. Even though the prepyloric region is often involved, pyloric stenosis is an unusual finding. The location of the lesion is known in 74 of the cases collected. Fifty-five of the cases involved one or both of the curvatures in the lower half of the stomach. Only six cases had pyloric stenosis. Three patients had lesions high in the cardia, one of whom complained of dysphagia. Ten cases were of the diffuse infiltration '*limitis plastica*' type.

These tumors may simulate at least two of the cell types found in lymphoid tissue—the small lymphocytes and the reticulum cells, which lend their names to the two types of lymphosarcoma encountered. Whether or not the parent cells of the follicles can give rise to a neoplasm has not been definitely established. Undoubtedly, these three cell types bear a close histogenetic relation to one another. Just what this relationship is, is not clear, as is demonstrated by the apparent change in cell type in some cases of giant follicular hyperplasia as they are followed throughout their course. However, in primary lymphosarcoma of the stomach a division into two types, lymphocytic cell and reticulum cell, seems adequate, and each type has its characteristic histology. In the lymphocytic type the cells resemble atypical lymphocytes in size and in the relation of nucleus to cytoplasm, and have deep staining hyperchromatic nuclei. At times there may be some variation in size, and cells nearly as large as mononuclear cells with a somewhat different nuclear arrangement are noted. Thus, the impression may be given of there being two cell types present. However, the small round cell resembling a lymphocyte is the predominant and distinctive one. Mitoses are frequent and often atypical. Multinucleated and "giant" cells are occasionally noted. Polymorphonuclear cells may be found scattered through the tumor tissue, but surrounding fibrosis and inflammatory reaction is usually not present, even though areas of liquefaction and necrosis are frequently found in the tumor.

The cells have not the definite connective tissue stroma that is the framework of a carcinoma, and even with special stains, only a fine, fibrous reticulum is demonstrated as the supporting structure. It is this character of the stroma

that accounts for absence of "shrinking" of the stomach and narrowing of the lumen with subsequent stenosis

All of the layers of the stomach wall may be entirely replaced by the tumor. Large areas may show no intact mucosa and only tiny remnants of glands will be found lying among masses of tumor cells. The muscularis mucosae is usually intact and is involved only in the most advanced cases.

In the reticulum cell type, infiltration of the layers may be present in a similar manner, but the predominant cells are cuboidal to polyhedral in shape, the nuclei hyperchromatic, and a large, well-defined cytoplasm is present. These cells may vary in size and shape in various parts of the tumor and are frequently bizarre in appearance. In some cases, a slightly more prominent fibrous framework is present. Usually the histology is just as distinctive as in the lymphocytic cell type. However, to differentiate some of these lesions from highly undifferentiated anaplastic carcinomata is sometimes very difficult, and the correct diagnosis can be inferred only from the subsequent course of the patient.

The perigastric and adjacent retroperitoneal nodes are the most frequent sites of extension. They are smooth and large and are relatively soft in contrast to the hard, more discrete metastatic nodes of carcinoma. Often they are matted together so that with involved omentum and areolar tissue, they make a mass larger than the original tumor itself. On section, the nodes are gray to pink and their structure appears completely lost. Metastases to liver, spleen and pancreas are found, but large nodules are infrequent. In Case 1, reported herewith, at autopsy, metastases were noted in perigastric, peripancratic, aortic, iliac, mesenteric and cervical nodes, omentum, pancreas, both ovaries, both lungs, pleura, diaphragm and peritoneum.

Since sarcomata, in general, are considered to have exclusively blood stream metastases, considerable discussion has taken place concerning the mode of extension of these tumors. Certainly this type of metastasis does occur in lymphosarcoma. However, the primary lymph node metastases must be considered as occurring by direct extension or metastasis through the lymphatics to the adjacent nodes. Tumor cells actually infiltrating the lymphatics of the stomach have been demonstrated in several cases.

Clinical and Laboratory Data—Careful evaluation of the clinical and laboratory findings reveals no single pathognomonic sign in the individual case. However, when taken as a group there are some suggestive points of differentiation. Pain of the ulcer type is a constant and often an outstanding symptom. "Dyspepsia" and anorexia are prominent findings, but a long history of anorexia with advanced emaciation is unusual. Some weight loss is the rule. Vomiting, if present, is usually not of the obstructive type, a finding which is easily explainable by the infrequent occurrence of pyloric stenosis. Hematemesis is not common, being noteworthy in but 12 cases in the present series. Straus (1925) believes it to be diagnostically significant in the presence of a nonobstructing tumor in a young patient. Melena is a frequent finding and occult blood was always found when a test was made for it. Perforation

of these lesions is considerably more frequent than with carcinoma. A palpable mass is present in almost two-thirds of the cases and is frequently quite large, in striking contrast to the absence of advanced emaciation in the patient.

There is no general agreement concerning the presence or absence of free hydrochloric acid. Douglas (1920) states that in the presence of a gastric lesion, youth and free hydrochloric acid are the most important factors suggesting a diagnosis of lymphosarcoma. In 17 of the 33 cases, in which gastric analyses are reported, the free hydrochloric acid was normal or elevated. This is a higher proportion than would be expected in a similar carcinoma series.

Roentgenologic Examination—The case of Balfour and McCann is the only* recorded case in which the diagnosis was made roentgenologically, preoperatively. There is a unanimity of opinion among most radiologists that there is no typical picture upon which to establish a positive diagnosis of lymphosarcoma. The lesion is most frequently mistaken for a carcinoma, and even in retrospect, the roentgenologic findings are often "typical" of carcinoma. It is also, at times, indistinguishable from peptic ulcer, particularly when a single "calloused" ulcer defect is noted in the prepyloric area on the lesser curvature.

If the history and clinical findings are taken into consideration, there are some suggestive points. Two or more defects in separate portions of the stomach should arouse suspicion, when they do not appear to be consistent with polyposis. In the presence of a large palpable tumor, instead of narrowing of the pylorus as with carcinoma, there may even be widening of the lumen. Rarely, these lesions when arising in the cardia may show roentgenologic evidence of extragastric penetration through the diaphragm. This is not found with carcinoma. Exaggeration of the mucosal folds to form giant rugae is seen, but this is not in itself diagnostic, however, when they are present and a filling defect is noted in a stomach with pliable walls, one has what is probably the most "typical" picture of lymphosarcoma.

Gastroscopy—Four cases have been observed through the gastroscope. None of these, however, was correctly diagnosed preoperatively. Schindler (1937) feels that the picture is sufficiently characteristic to enable him to make the diagnosis in the future.

Treatment—Radical, subtotal gastrectomy followed by intensive deep radiotherapy has usually been considered the treatment of choice. Operation is contraindicated only in those patients who are obviously in the last stages of the disease. Even then some effort should be made to establish a histologic diagnosis. This point is emphasized because of the marked regression following radiation, sometimes seen, in patients who appear to have a far advanced gastric neoplasm. Zanetti's case (1935) appeared to be in excellent health and showed no roentgenologic evidence of disease, two years after presenting himself with an apparently hopelessly advanced lesion. Undoubtedly, a number of patients with lymphosarcoma have died with the diagnosis of carcinoma. Had the correct histologic diagnosis been established, it is reasonable to assume

* Case of Escudera, quoted by Gomez y Gomez (1931) and referred to by Bastony (1935) was not available for study.

that a few of these might have received at least palliation. In very sick patients and where tissue examination is impossible a therapeutic trial with radiation seems justifiable.

The Pólya type of resection, with whatever modifications the surgeon is best acquainted, is well suited to the disease unless the situation or extent of the lesion requires complete gastrectomy. Since radiation stands as an effective subsequent means of treatment, resection should be performed if technically feasible, even if it appears questionable that all the local extension of the disease can be completely removed. Palliative procedures, such as gastroenterostomy, are rarely indicated, since stenosis is quite unusual and because radiation is of more value.

In this series of 152 cases, celiotomy was performed in 118 patients. Seventy-six of these had subtotal gastrectomy performed, with 12 postoperative deaths—an operative mortality of 15.8 per cent. This 50 per cent resectability is much greater than carcinoma and the operative mortality somewhat less.

It is exceedingly important to administer the roentgenotherapy carefully. Due to the marked intolerance to radiation over the epigastrium, only relatively small amounts can be given under the most favorable circumstances. The exact site of the lesion, with the patient in the position he is to assume during treatment, should be determined by barium meal and the corresponding area delineated on the abdominal wall. This is essential in order to deliver the maximum radiation directly to the lesion. Nausea, anorexia and "burning" distress may be so marked as to preclude further therapy if it be poorly directed or if too large daily doses are delivered.

Scaled, fractional doses over a period of 25 to 35 days are considered the optimum plan of therapy. As Pack and McNeer (1935) recommend, the radiation is best delivered to the outlined lesion through three portals, left anterior, left posterior and left lateral. Between 50 and 100 r is given at each sitting, depending upon the tolerance of the individual patient. A total tumor dosage between 2,500-4,000 r is desirable. If marked improvement results, but the disease remains, demonstrable clinically or by gastro-intestinal series, a second and third series may be administered at intervals of from six to eight weeks or more. When the tumor seems to be susceptible and gross metastatic lesions are noted, these should also be radiated.

Radiation of hollow viscuses containing large ulcerating tumor masses always entails the real danger of gross hemorrhage. For this reason, Holmes (Cabot Case, 1934) endorses resection whenever possible before radiation. However, Pack and McNeer (1935), while acknowledging the danger, have not had this complication in treating a number of patients with irremovable lesions. The possibility of producing adrenal insufficiency with radiation in this area has been also noted, but it has been shown that this probably does not occur unless the gland is already the site of neoplastic infiltration.

Undoubtedly, radiation has secured remarkable results with regression of all signs of the growth for long periods—if not actual "cures." However, the

degree of radiosensitivity of the growth, apparently, is not predictable from the study of the pathologic material. Thus, a far advanced growth may react favorably for a number of years to what is generally considered inadequate treatment, while an apparently favorable one will rapidly come to fatal termination with excellent therapy. This suggests that these lesions have a life history independent of the type of therapy administered and what appears to be "curative" treatment may be only coincidental in the "natural" course of that particular neoplasm.

Results—Including two cases from this hospital, 13 of the 152 cases were living and well 5 to 22 years after the diagnosis had been established. A brief synopsis of the essential data relevant to the 11 cases reviewed is appended.

No 1—Cheever, D (1932) Female, age 52, had a segmental resection of middle third of stomach. Pathologic Report Lymphocytic cell lymphosarcoma. Two roentgen ray treatments were given postoperatively. Living and well five years later.

No 2—Pack, G, McNeer, G (1935) Case 5 Female age 46, complained of pain and dysphagia. Bulky tumor involving parts media and crura found at operation. Biopsy Reticulum cell lymphosarcoma. With radium pack, 48,000 mg hours was given at a distance of 15 cm, anteriorly and posteriorly to cross fire the stomach. Living and well six years later.

No 3—Pack, G, McNeer, G (1935), Case 7 Male, age 53 was operated upon by Dr S Harvey, had a segmental resection of the prepyloric area. No roentgen ray treatment. Pathologic Report Lymphocytic cell lymphosarcoma. Living and well 7½ years later.

No 4—Collins, E, Carmody, M (1937) Male, age 9, had a partial gastrectomy and posterior gastroenterostomy. No roentgen ray treatment. Pathologic Report Lymphocytic cell lymphosarcoma. Living and well 22 years later.

No 5—Falta, W (1926) Male age 55, had a subtotal gastrectomy and gastroenterostomy. Line of resection, distally, went through what was considered a "peptic ulcer." Pathologic Report Lymphosarcoma. Immediate intensive radium treatment. Five other treatments in next 24 months. Two "prophylactic" exposures to radium later. Living and well 6¼ years postoperatively.

No 6—Clar, K (1935) Male, age 22, had a Bilroth II Hoffmeister resection of the stomach. No roentgen ray treatment. Pathologic Report Lymphocytic cell lymphosarcoma. Adjacent excised nodes showed only hyperplasia. Living and well seven years later.

No 7—Gunsett, A, Oberling, C (1928) Male, age 48, had a prepyloric tumor penetrating through to pancreas with many metastatic nodes on lesser curvature. Biopsy and anterior gastroenterostomy. Pathologic Report "Pure" lymphosarcoma. Received 17 radiotherapy treatments in three weeks for a total of 26 hours. A total of 12,700 (French) r given anteriorly, posteriorly and from both sides at a distance of 40 cm through 1 Mm of copper at 2.5 ma. Living and well at five years. G I series negative for recurrence.

No 8—Weeden (1929), Gibson (1927) Male, age 34 had pain in epigastrium six months coming on one hour after eating. Weight loss 20 lbs. Operative Pathology A mass size of palm of hand in posterior surface of stomach with enlarged nodes. Operation—Distal one third of stomach resected (Gibson pylorotomy). Pathologic Report Lymphosarcoma. In excellent health nine years later.

No 9—Leriche, R, Irman, E, (1929) Male, age 43, had epigastric distress one year previously at which time a G I series was negative. Recurrence of pain with weight loss and appearance of large mass in right epigastrium. Operative Pathology A large tumor of the antrum with extension on lesser curvature. Operation—Polya resection with anterior gastroenterostomy. Pathologic Report Lymphosarcoma of stomach. Well for six years, when epigastric distress recurred. Roentgen ray suggested gastrojejunal ulcer. Operation—Gastrotomy. No trace of original disease or ulcer. Discharged in good health six years and six months after operation for original disease.

No 10—Kaiser (1934) Female, age 51 had pain in left epigastrium. Weight loss 6 Kg. Hard mass beneath left costal margin. G I series showed tumor arising from greater curvature in upper third of stomach. Operation—Biopsy only, as mass was too large to remove. Pathologic Report Lymphocytic cell lymphosarcoma. Muscle is infiltrated but serosa is not involved. Patient received three roentgen ray treatments over a period of three months to a field 18x18 cm. The radiation was delivered by a 200 KV machine at 2.5 ma with 1.3 Mm Cu and 1.0 Mm Al filter. Between 70 and 77 per cent of the skin erythema dose was delivered to the tumor. G I series in 1928 and again in 1929 were negative for persistence of disease. Patient is living and well eight years after biopsy.

No 11—Ruppert (1912) (Shopf) Female, age 57, had a complete gastrectomy for a diffuse infiltrating lesion. Pathologic Report Typical infiltrating, primary endogastric lymphosarcoma. In situ, and well 14½ years later, with negative G I series. Small intestine was shown to have pouched out considerably and served as a temporary food reservoir.

LYMPHOSARCOMA OF STOMACH

RESUME OF FIVE CASE HISTORIES FROM THE PRISBYTERIAN HOSPITAL, N. Y.

Case 1—No 222365 F F, White, female, age 48, married, was admitted to the hospital April 16, 1934, complaining of swelling and distention of abdomen for three weeks. For years had been troubled with "indigestion" and gas, especially following fatty foods. For the last three weeks patient had noted abdominal swelling with feeling of pressure in epigastrium relieved by belching. She had had anorexia for last four days. Her bowel habit was regular and stools normal. She had lost a small amount of weight. Orthopnea had been noted for the past two days.

Physical Examination—Revealed a poorly developed, chronically ill woman. Almond-sized hard node palpable in right supraclavicular fossa. No general node involvement. Lung signs were compatible with a right hydrothorax. The abdomen was greatly distended and tense. There was shifting dullness. Pitting edema in both legs. Hemoglobin



FIG 1—Case 1. The stomach specimen showing the smooth nonulcerated mucosa and the diffuse infiltration (limitis plastica) of practically the entire stomach.

80 per cent, R. B. C. 4,250,000, W. B. C. 7,850, polys 82, lymph 9, monos 7, eosinophils 1, basophils 1, urine negative, Wassermann negative.

Roentgenologic examination of chest showed right hydrothorax and some evidence of congestion on the left but no absolute evidence of metastases. A G. I. series demonstrated an extensive growth involving the entire lesser curvature—a "saddle growth" extending around posteriorly and anteriorly. Surgically she was felt to be a far advanced case of malignant disease with the stomach as primary focus, and the outlook hopeless. Temporary relief was obtained by paracentesis and thoracentesis. The fluid obtained contained cells about the size of large lymphocytes with dark ground glass cytoplasm and a round dark nucleus filling about half the cell. Some cells were in mitosis. She died suddenly just before discharge to a home for incurables. *Clinical Diagnosis* Carcinoma of the stomach with metastases to peritoneum, pleural cavities.

Autopsy—No 11538 Dr A. Longacre. *Pathologic Examination* Gross "The stomach wall is markedly thickened and firm throughout, except for a small area near the cardia. On the lesser curvature there are several large nodular masses (lymph nodes) covered with peritoneum which appear continuous in places with the gastric wall. On section they consist of white, granular tissue with areas of necrosis. On opening the stomach the mucosal surface is smooth, except for some areas where distinct ridges are present (Fig 1). No ulceration is seen. On section the markedly thickened mucosa is seen infiltrated with grayish tissue which in places extends through the entire thickness of stomach. Gross evidence of metastases are seen in regional lymph nodes, pancreas, omentum and diaphragm and small foci in pleura, ovaries and cervical nodes."

Microscopic—The mucosa, submucosa, muscularis and serosa are densely infiltrated with tumor cells. The cells are predominantly of two types—a round cell the size of a small lymphocyte with dense hyperchromatic nuclei surrounded by narrow zone of basophilic cytoplasm (Fig 2). The other is about the size of a mononuclear with homogeneous, acidophilic cytoplasm. An oval nucleus is situated at a pole or along one side of the cell. Mitoses are frequent. A rare giant cell is seen. There is practically no stroma (Fig 3). There are many capillaries. The mucosa shows some autolysis and replacement of some of the glandular elements with tumor. Muscularis mucosa is intact. Submucosa is markedly increased in width. The muscle fibers are separated by masses of tumor cells. The serosa is thickened by tumor infiltration.

Note by Dr A M Pappenheimer "A very characteristic lymphosarcoma of the stomach, which infiltrates the entire viscus as well as the regional lymph nodes, pancreas, omentum and diaphragm. There are small metastatic foci in the pleura and ovaries. The tumor cells are for the most part not highly atypical. Many of them closely resemble small lymphocytes, but there is an admixture of larger elements."

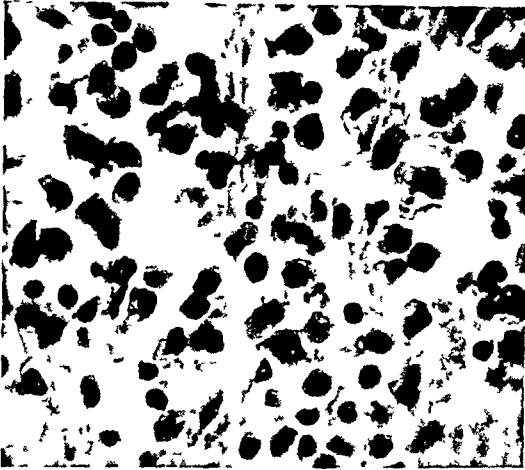


FIG 2—Case 1. Photomicrograph of a section of stomach. The predominant cells resemble small lymphocytes with hyperchromatic nuclei. There is an admixture of larger elements with eccentrically placed nuclei ($\times 700$).

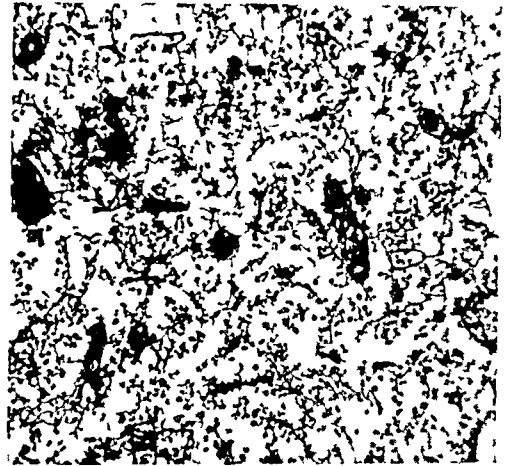


FIG 3—Case 1. Same section as Fig 2, with reticulum stain clearly demonstrating the sparsity of stroma ($\times 150$).

This is an example of Type IV in Pack's and McNeer's classification, showing diffuse thickening of the wall, much like a "limitis plastica" lesion. Microscopically it is of the lymphocyte type of lymphosarcoma. Undoubtedly little could be done therapeutically for this particular patient, but it serves to demonstrate how easily a lymphosarcoma of the stomach may go on to fatal termination with a histologically unproven diagnosis of "typical carcinoma with metastases."

Case 2—No 230783. T. M., Negro, male, age 40, married, was admitted to the hospital June 18, 1935, complaining of abdominal pain for two months. He had always enjoyed general good health. "Blood tests" were said to be negative, but he had received some intramuscular injections. He had had crampy pain in the epigastrium for two months, usually coming on 15 minutes p.c. and relieved temporarily by food. He was told he had an ulcer one month before (no roentgen ray examination was done). Prescribed diet and powders had failed to relieve pain. Had vomited for first time four days before admission. Tarry stools were noted several times in the last six days.

Physical Examination—Patient did not appear acutely ill. No superficial lymphadenopathy. The abdomen was not distended or tender. A lemon-sized mass was

palpable in the epigastrium just to the left of the midline. There was no hepatosplenomegaly. Hb 82 per cent, R B C 3,970,000, W B C 6,760, P 81, L 18, M 1. Urine negative. An Ewald test meal showed free HCl 38, total acid 55. Stool had a 4+ guaiac. Wassermann negative.

Roentgenologic examination of the stomach showed 100 per cent six-hour retention, and nothing could be forced through pylorus. The antrum was fixed, tender and inflexible and showed no peristalsis. Impression. An extensive carcinoma of the antrum, invading and involving pylorus (gastric lues was considered a possibility).

Operation—June 25, 1935. Under spinal anesthesia patient was explored by Dr. J. F. Roberts through a transverse incision. A rounded elastic tumor was found involving the pylorus and extending up on lesser curvature. Posteriorly it was bound down to the pancreas. There appeared to be infiltration by tumor of the gastrohepatic omentum. Several small perigastric nodes were palpable. A resection seemed inadvisable, and a posterior isoperistaltic gastrojejunostomy was performed. He had a smooth postoperative course, except for some evidence of atelectasis on second day. Examination by Dr. V. F. Frantz of the specimen removed from gastrohepatic omentum showed it to be simply a peritoneal band with some fibroblastic proliferation. The question was raised whether the changes might be due to syphilis. Patient was discharged July 14, 1935 on an ulcer diet and was to receive antiluetic treatment.

Subsequent Course—He was relieved of pain during the following month, but despite antiluetic treatment, the lesion in stomach progressed to involve the duodenal bulb. Roentgen ray diagnosis, August 1, 1935, was carcinoma of antrum, probably not lymphoblastoma. He was readmitted for attempt to resect, in view of the negative biopsy.

Second Operation—August 8, 1935. Under spinal anesthesia, Dr. J. F. Roberts demonstrated a stony-hard tumor involving the lower half of the stomach and upper portion of duodenum. It was adherent to the adjacent structures and to the old incision. The lesion extended to within 4 cm. of the old posterior gastro-enterostomy. Lymph nodes seemed to be free of disease. The first part of the duodenum and the stomach were resected up to the old posterior gastro-enterostomy. The patient had an unusually smooth postoperative course and was discharged September 4, 1935. Readmitted October 12, 1935, because of evidence of wound infection. This was relieved by instituting adequate drainage. Roentgenotherapy was begun September 3, 1935. G. I. series, February 10, 1936, was negative for recurrence. Readmitted April 30, 1936, complaining of pain in lumbar region and right flank. The abdomen was distended, and a sizable mass was palpable in midabdomen. Some abnormality of the right kidney was shown by retrograde pyelogram but surgery was not advised. Patient continued downhill after discharge April 18, 1936, and died June 1, 1936.

Roentgenotherapy—September 3, 1935 to December 18, 1935. Received 2,300r through an anterior portal over the stomach to area 10x10 cm., in divided doses of 100-150r. The factors were 190 K V, 50 cm T S D, 8 m a, filter 0.5 Mm Cu + 1 Mm Al. 600r was given through each of two portals over palpable recurrences, between April 8, 1936 and May 5, 1936. The factors were 190 K V, 50 cm T S D, 8 m a, filter 1.86 Mm Cu + 1 Mm Al.

Pathologic Examination—Dr. F. M. Smith. *Gross*. The peritoneal surface is smooth and contains no suggestive tumor nodules. A portion of pancreas is adherent to the posterior wall near pylorus. On opening the stomach, it is seen to be almost entirely filled by a large, smooth spongy tumor completely denuded of mucous membrane (Fig. 4). The line of resection is within 0.5 cm. of the proximal line of resection. The tumor is elevated above the normal mucous membrane and in the antrum completely encircles the lumen. It has grown in such a manner as to form a crater-like depression at one point, where there is ulceration. Subadjacent to this there is a large area of necrosis in the tumor. In some areas the tumor has attained a thickness of 2 cm. and has infiltrated all of the layers except the serosa. *Microscopic* section shows a small round cell tumor which has replaced nearly all elements of stomach wall (Fig. 5). Occasional fragments

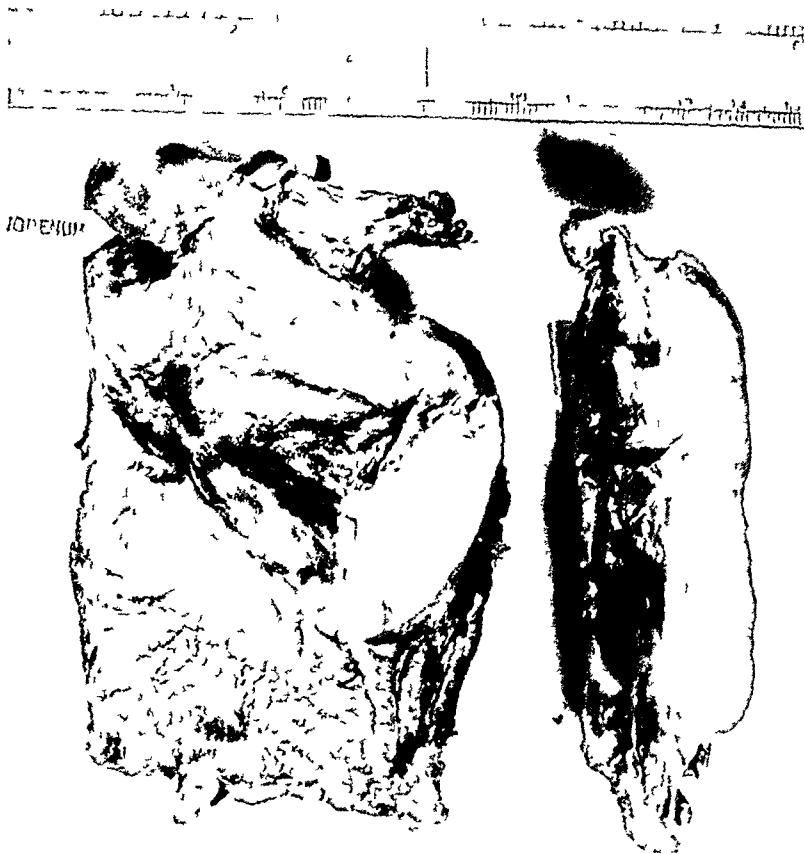


FIG 4—Case 2 Stomach specimen There is marked thickening of the antrum where the tumor completely encircles the stomach. Ulceration and necrosis is clearly seen in the crater like center of the tumor. Attached duodenum appears uninvolved. The cross section, on the right, shows the enormous thickening of the wall.

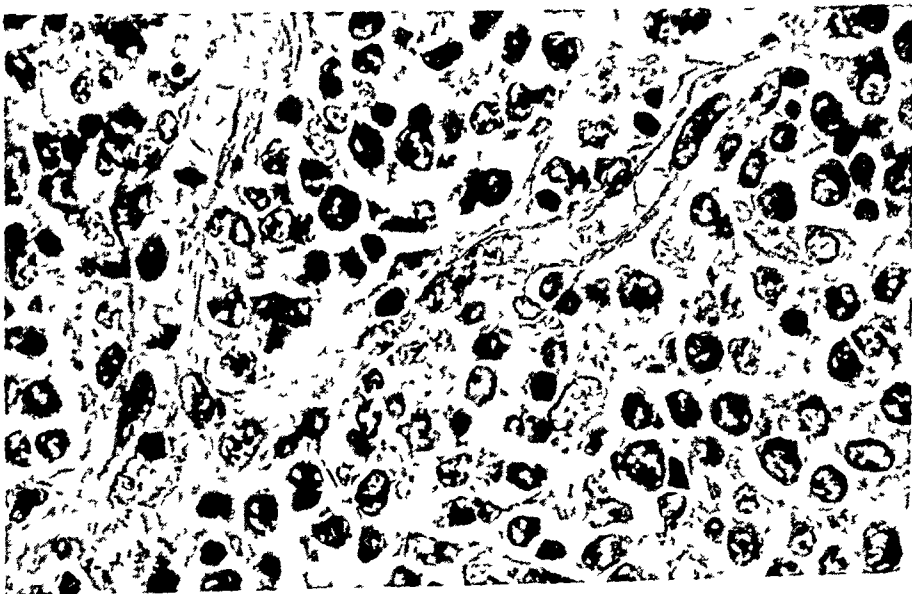


FIG 5—Case 2 Photomicrograph of a section of the stomach clearly demonstrates the morphology of the normal tumor cells lying in a scant supporting framework ($\times 1100$)

of mucous membrane and nests of acid glands are seen, and nearly all of the muscle is replaced. The serosa is involved, but the lymph nodes are not. The tumor invades up to the line of resection. The individual cells are the size of small lymphocytes with a small amount of clear cytoplasm and hyperchromatic nuclei, often eccentrically placed. There is little supporting stroma and practically no fibrosis nor inflammatory reaction. There are some areas of liquefaction necrosis.

This is a lymphocytic cell type of lymphosarcoma of the bulky polypoid variety. The difficulty of making a correct diagnosis of the disease, even upon direct examination, is well brought out. The roentgenologist's note concerning the flexibility of the walls is perhaps the only suggestive finding, even in retrospect. Microscopically this appeared to be a radiosensitive tumor, yet the amount of roentgenotherapy given presumably did little but relieve pain, and death ensued within 10 months after resection.

Case 3—No 222561 I K, female, age 36, married, was admitted to the hospital September 13, 1933, complaining of loss of weight, weakness and vomiting for one year. First admission, September 18, 1929, was for partial thyroidectomy for adenoma of thyroid. March 10, 1932, at second admission, had a full term spontaneous delivery at which time added diagnosis of fibromyoma of uterus was made. First G I symptoms were in 1930, with vomiting p. c. without pain. A G I series, December 22, 1930, was suggestive of an anomalous first part of duodenum possibly associated with gallbladder disease. January 2, 1931, gallbladder dye series was negative. Patient continued to have distress intermittently despite a dietary regimen but went through a second pregnancy in 1931-2. She developed more distress and anorexia during February, 1933. A second G I series was done March 5, 1933. Peristalsis was present only on the greater curvature and was irregular. The prepyloric region appeared narrowed. This was first considered an early sclerotic type of carcinoma, but a review of films did not substantiate this point and the patient was placed on a diet. She continued to have vomiting, anorexia and began to lose weight. A gastric analysis showed free HCl 16, total acid 29. Another G I series demonstrated the picture of advanced carcinoma of stomach involving the posterior wall and greater curvature, in the pars media, "a surprising amount of mobility is present in considering the size of the associated mass." Patient was readmitted September 13, 1933. Hb 62, R. B. C. 3,970,000, W. B. C. 13,300, P 81, L 16, M 3, Stool guaiac 4+. No free HCl found in gastric expression.

Operation—September 18, 1933, through a left paramedian incision under spinal anesthesia a Polya type of partial gastrectomy with posterior gastro-enterostomy and entero-enterostomy was performed by Dr. F. Meleney. Her postoperative course was uncomplicated. She was discharged to a convalescent home on the twenty-fourth postoperative day.

Subsequent Course—Readmitted October 31, 1933, complaining of abdominal cramps for two days and back pain. She appeared quite weak and emaciated. A questionable mass was palpated in the left upper quadrant. A G I series showed no definite evidence of recurrence. The severe cramps were relieved by roentgenotherapy and patient discharged November 23, 1933. Presented herself March 7, 1934, two months pregnant. A therapeutic abortion was performed March 17, 1934. She did well until May 2, 1934, when cramps returned and she began to have difficulty in swallowing. A routine G I series was equivocal, but a thick meal showed narrowing and distortion of the esophagus at the cardia, which was considered to be a recurrence in the wall of the esophagus. Partial relief followed roentgenotherapy until September 1, 1934, when vomiting and difficulty in swallowing precluded all eating. A definite mass noted in epigastrium, and a G I series showed multiple defects in stomach. She could tolerate no further roentgenotherapy and was referred for terminal care. She died October 26, 1934, 13 months after operation.

Röntgenotherapy—November 15, 1935 to January 19, 1934 Received 1,800r in divided doses of 100-120r through anterior portal to area 15x15 cm over mass The factors were 180 K V, 50 cm T S D, 4 m a, filter 0.53 Mm Cu and oil Subsequently (February 2, 1934 to February 23, 1934) a similar field over suspected mass below

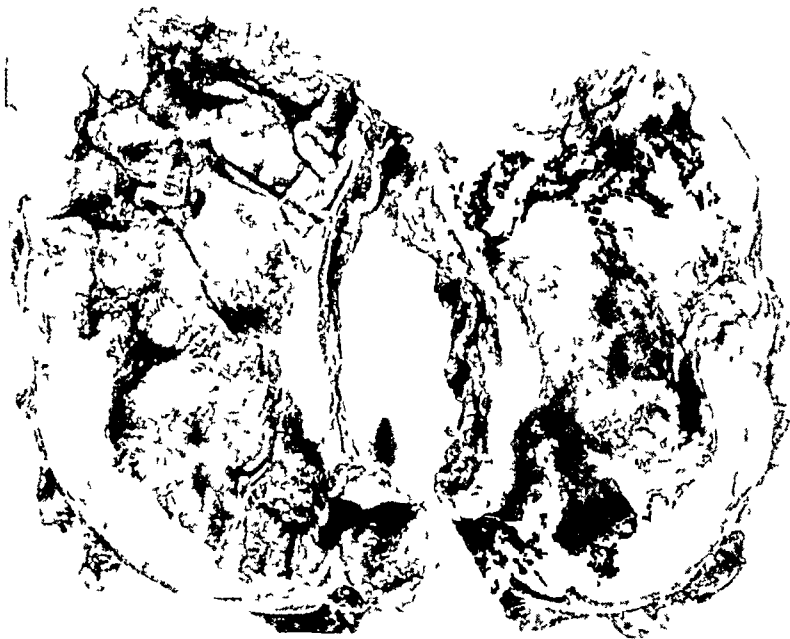


FIG 6—Case 3 Operative specimen with stomach bisected and pylorus below, shows involvement of practically the entire greater curvature and a portion of the lesser curvature The extent of the thickening of the wall is clearly seen

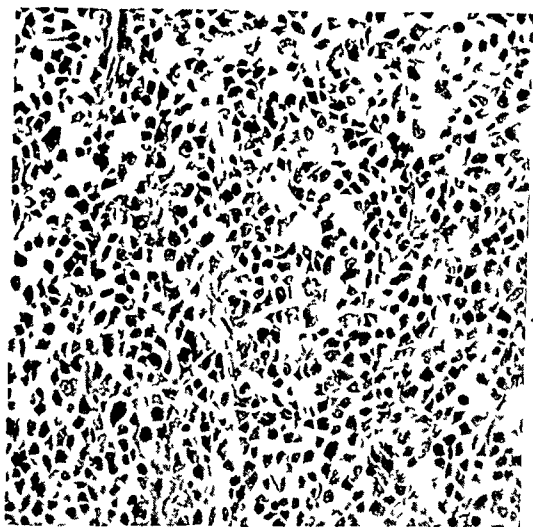


FIG 7—Case 3 Photomicrograph showing that the polygonal tumor cells are seen to vary somewhat in size but resemble the reticulum cell of the lymphoid system No tendency to acini formation is observed (X500)



FIG 8—Case 4 Gross specimen of the stomach as removed at operation Specimen bisected with pylorus at the top The massive bulky tumor is seen to be fairly well demarcated from normal mucosa as the cardia is reached

and to left of original area received 600r The factors were 190 K V, 50 cm T S D, 8 m a, filter 0.55 Cu + 1 Mm Al In May, 1934, 625r were given anteriorly to area corresponding to esophageal and cardiac involvement An incomplete series was given just before patient's death in September, 1934 In all, 4,800r were given in six series over a period of seven months

Pathologic Examination—Dr A P Stout *Gross* There is a large soft nodular tumor with a superficially ulcerated surface which extends from the pyloric ring for a distance of 10 cm along the lesser and 17 cm along the greater curvature, completely encircling the stomach (Fig 6) The thickness varies from 5 to 20 Mm and in most areas the muscle coat although invaded has not been completely penetrated The tumor appears to end abruptly just as the pyloric area is reached, and resection is ample as a part of duodenum is excised distally *Microscopically*, there is disease one millimeter from proximal line of resection The tumor cells are polygonal and vary greatly in size and shape (Fig 7) The nuclei are hyperchromatic and the cytoplasm is well defined and amphophylic There are many mitoses The cells are arranged in foliate pattern in a delicate reticulum with no tendency to form acini The lymph nodes removed contain sinuses dilated with lymphocytes and polygonal cells similar to the tumor cells in stomach

This is a lymphosarcoma of the reticulum cell type Unfortunately, there was some question on first examination whether or not it was an anaplastic carcinoma, and for this reason there was a delay in administering roentgenotherapy

Case 4—No 81486 J M K, male, age 64, married, was admitted to the hospital April 17, 1929 Always had general good health in past, except for "hunger pain" for 20 years In 1925, had pain low in abdomen, not related to eating but relieved by soda and food In 1927, began to lose weight and vomited occasionally A diagnosis of ulcer was suggested, without roentgenologic examination Patient gained 20 lbs after nine weeks of diet and bed rest Patient had hematemesis and tarry stools in September, 1927 and he was in bed six weeks He remained asymptomatic until December, 1928, when the pain recurred Had a remission again until April, 1929, when the pain recurred Patient had had a hematemesis the day before admission On admission he complained only of "gas" and epigastric pain Physical examination was equivocal except for some pallor and abdominal distention There were no signs of shock He was placed on bleeding ulcer regimen with nothing p o, and given hypodermoclyses and rectal instillations Hb 43 per cent, R B C 3,460,000, W B C 13,050, P 74, L 24, M 2 Urine was essentially negative He showed no evidence of further gross hemorrhage and was placed on a modified Sippy regimen, April 19, 1929 He improved slowly, having pain only at night Stools on five consecutive days were negative to guaiac Gastric analysis showed a free HCl 14, total acidity 54 On May 15, 1929, a G I series demonstrated a broad incisura on the greater curvature of the stomach with narrowing of lumen to about one centimeter The lesser curvature in this region was somewhat irregular Peristalsis was present above and below this region but did not pass through it Stomach walls were quite flexible There was a 25 per cent gastric retention at six hours "Findings are those of gastric ulcer" He received four transfusions 600-800 cc, which brought his Hb up to 100 per cent However, he continued to show some gastric retention and, June 4, 1929, a second G I series showed the marked constriction persisted and a small projection was noted on the lesser curvature side at this point There was a six-hour retention of 50 per cent He was discharged with diagnosis of gastric ulcer

Subsequent Course—He was readmitted, November 12, 1929, as he had episodes of severe pain during summer months Stool examinations were persistently positive for blood He also had had one small hematemesis A recent G I examination showed a large, greater curvature crater which suggested carcinoma Hb 88 per cent, R B C 4,770,000 He had had no weight loss Because of the persistence of bleeding and the roentgenologic findings, operation was decided upon

Operation—November 13, 1929 Under spinal anesthesia and drop ether, the abdomen was explored through a T-shaped incision, by Dr A O Whipple A large ulceration was found on greater curvature with infiltration on lesser curvature and posterior wall extending well to the cardia Although it appeared almost impossible to get above

the lesion, which was considered to be a carcinoma, it was decided to resect in view of absence of metastases in liver and adjacent lymph nodes. A Bilroth II with gastrojejunostomy and entero-enterostomy was performed. A drain was placed down to duodenal stump because of insecure inversion. A 700 cc transfusion was given postoperatively. Smooth course postoperatively, except for development of gastric fistula on the eighth day. This was exceedingly bothersome often draining 1,500 cc in 24 hours, it, however, healed slowly and the patient was discharged in generally good condition on the thirty-eighth postoperative day. He subsequently developed a large ventral hernia.

Pathologic Examination—Dr A P Stout Gross. The stomach is rather bulky and rounded. Peritoneal surface is smooth. On opening the organ just above the pylorus, the wall becomes suddenly thickened to 16 Mm (Fig 8). This thickening encompasses the entire circumference and extends along the lesser curvature for 2 cm and the greater curvature for 5.5 cm.

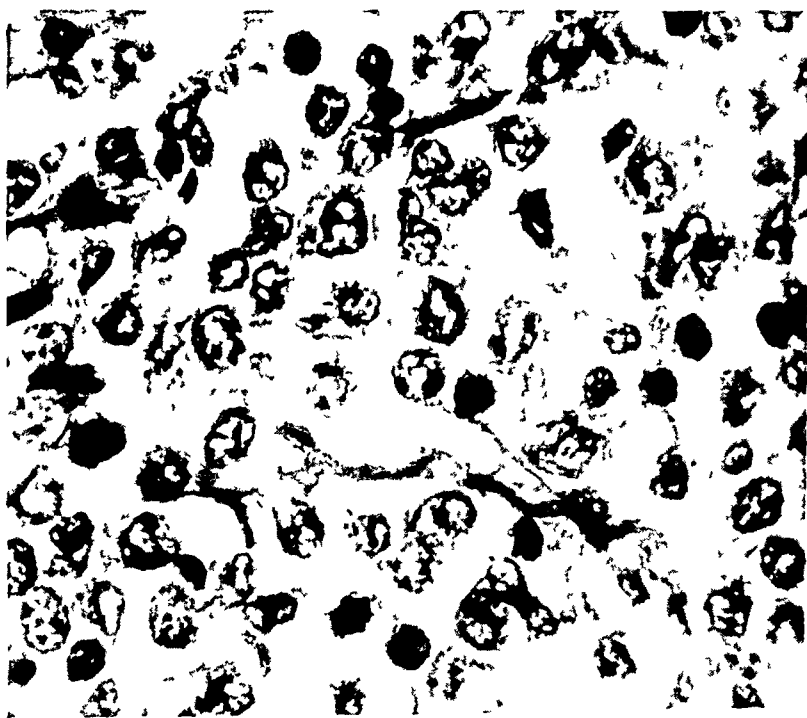


FIG 9—Case 4. Photomicrograph of a section through the tumor, showing the tumor cells, cuboidal in shape and having large hyperchromatic nuclei. There is very little supporting framework. (X1100)

Microscopic—A section through tumor mass shows that it is composed of solid masses of small cuboidal cells separated by fibrous tissue strands (Fig 9). An unusual power of infiltration is noted without corresponding destruction. The individual cells are hyperchromatic with large nuclei and small cell body. Mitoses are frequent. The mucous membrane retains semblance of its architecture but tumor tissue widely separates the glands. There is no attempt at gland formation by the tumor cells. Tumor cells are noted in lymphatic spaces. Proximal line of resection goes through tumor bearing tissue. Only a very fine supporting framework is noted with special stains. *Pathologic Diagnosis* Anaplastic carcinoma (?) of stomach.

At no time did this patient receive any roentgenotherapy. He had been regularly followed and repeatedly examined by his personal physician, and when last seen, October 26, 1937 at the age of 73, he was in excellent health and showed no evidence of recurrence—eight years after operation.

This lesion exemplifies the massive bulky type of growth fairly well demarcated from the normal stomach. In retrospect nothing in the symptoms or roentgenologic findings particularly suggested the correct diagnosis.

On reviewing this case in 1934, it was felt that the pathology was that of a reticulum cell lymphosarcoma as was originally suggested by the sarcomatous appearance of the gross specimen. As the patient had remained in excellent health for five years, no roentgenotherapy was suggested.

Case 5—No 268878 F M, male, age 19, was first seen, February 4, 1931, following an attack of syncope associated with body tremors but no actual convulsion. A subsequent neurologic examination was negative, except for hypertension (170/90). Patient showed definite antisocial tendencies and "a type of personality that is always on the defensive." He stated that the convulsive-like seizure was always preceded by right lower quadrant pain. He was seen December 28, 1931 in clinic, complaining of epigastric distress p.c. for two months, partially relieved by food. He had lost 10-20 lbs. He had had a previous operation for right undescended testicle, November, 1928, and an appendectomy, November, 1929.

Physical Examination showed pallor of face and mucous membrane (blood donor). Carious teeth. Blood pressure 120/70. Abdomen was negative. Hb 63 per cent, R B C 3,900,000, W B C 6,200, P 57, L 35, M 3, E 5. Chest film negative. Scout film of abdomen was negative. Wassermann negative. January 5, 1932, three hours after a G I series, patient showed typical signs of perforation of a hollow viscus. *Preoperative Diagnosis*—Perforated gastric ulcer.

Operation—Dr. D. Bull. A perforation was found on the anterior surface of the stomach in the prepyloric area, with induration extending 10 cm proximally and 4 cm distally. Ridged, indurated, enlarged rugae were palpated along the posterior wall through the perforation. A number of enlarged nodes suggestive of neoplastic involvement were palpable. A biopsy of the stomach wall and a lymph node were taken and a simple closure of the perforation was performed, with a free omental graft. He had a very smooth postoperative course. A review of the G I series showed a constant incisura at the great curvature near the antrum, with mucosal folds so exaggerated as to give an almost polypoid appearance.

Pathologic Examination—Dr. A. P. Stout. *Microscopic*—The stomach biopsy shows an extensive inflammatory reaction. There are many tumor cells varying considerably in size and shape. An occasional mitosis is seen. There is no tendency to glandular arrangement. The cells do not form mucin. Many of the cells have the characteristics of lymphoblasts (Fig 10).

The lymph node shows practically complete replacement with tumor cells similar to those in stomach wall. Mitoses are more frequent than in stomach specimen. The connective tissue stroma is meager, but there is slightly more than usually found in lymphosarcoma (Fig 11).

It was felt from the stomach specimen that this was a highly malignant tumor—either anaplastic carcinoma or a reticulum cell lymphosarcoma. The lymph node, however, was so characteristic of reticulum cell lymphosarcoma that there was no doubt as to the diagnosis and plans for roentgenotherapy were made. After five treatments the patient decided to go away for a rest. He returned, February 17, 1932, and was given a course of 10 treatments.

April 16, 1932, six hours following one of the patient's unconscious spells, he was seen in the Admitting Clinic with typical signs of perforation. An immediate operation by Dr. Bull demonstrated a perforation similar in location to the first one. Because of the dense adhesions and the patient's poor condition, no biopsy or exploration was done. Closure of perforation was easily accomplished by plication, and the abdomen closed.

without drainage. Again, he had an exceptionally smooth postoperative course, and was discharged May 1, 1932.

The patient was very refractory to treatment and refused any further roentgenotherapy.

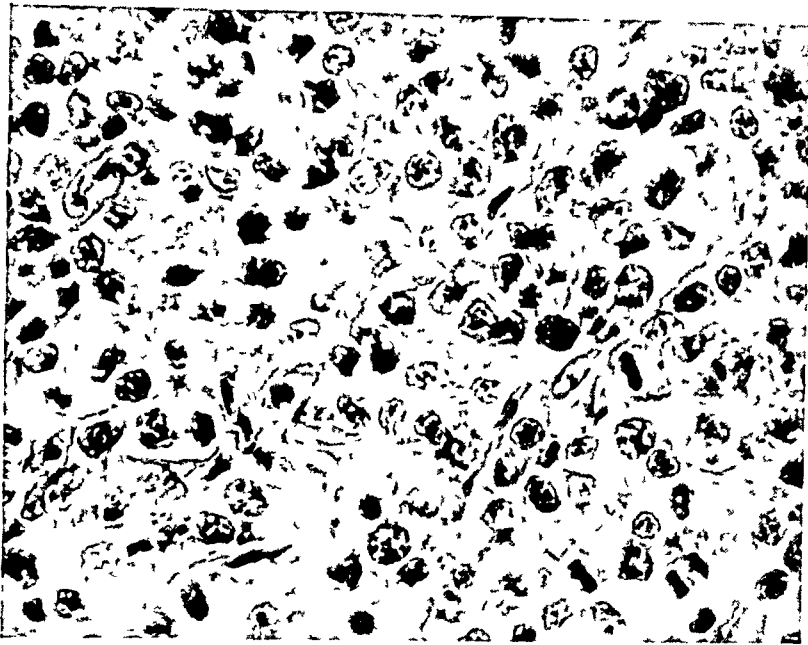


FIG 10—Case 5 Photomicrograph of a section of the stomach wall at site of perforation. Note absence of inflammatory reaction. Tumor cells, resembling those of the lymphoblast series, are seen to vary considerably in size and shape. Mitoses are frequent. There is no tendency to glandular arrangement. ($\times 1100$)

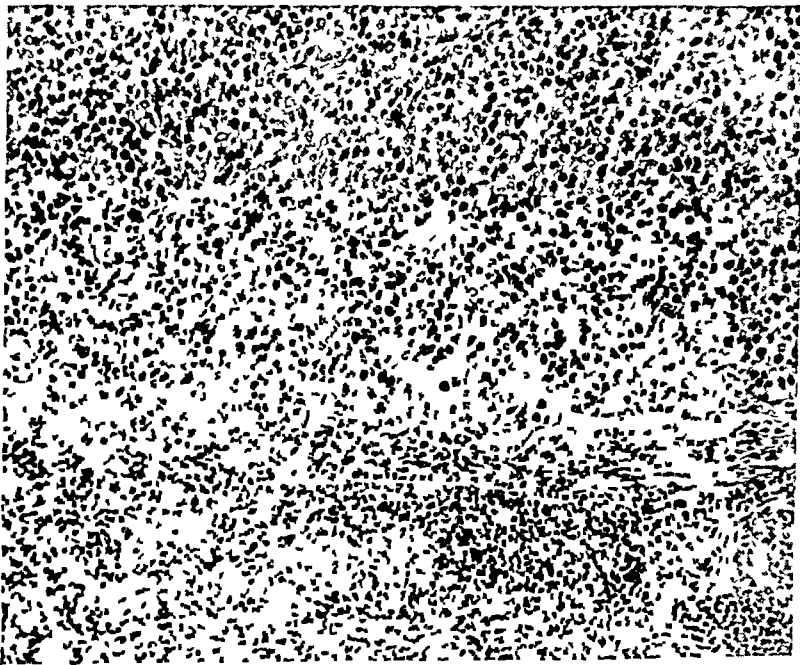


FIG 11—Case 5 Photomicrograph of a section of the lymph node demonstrating the dense infiltration of the tumor cells above, in contrast to the normal lymphoid tissue below. ($\times 250$)

A G I series was done, March 29, 1933, and showed a constant incisura along greater curvature near the antrum. This was attributed to postoperative scarring. G I Series done April 9, 1934, showed no change in the findings. He continued to do fairly well notwithstanding complete disregard of diet, smoked excessively, and drank freely.

June 12, 1934, he was again admitted for abdominal pain. Abdominal cramps had appeared previously, associated with nausea and vomiting. Bowel movements had been only clear fluid for the previous 48 hours. Three-position roentgenograms of the abdomen confirmed the clinical impression of ileus. He was completely relieved by rectal treatments and parenteral fluids.

The patient continued to do well on a dietary regimen until September 1, 1935, when he again developed abdominal cramps, which were relieved by rectal treatments. A G I series, February 20, 1937, gave the impression that there was some thickening of the antral wall, because of decreased activity and some interruption of peristalsis in this region.

He was last seen, September 3, 1937, by a social worker, who found the patient in good health. He had married, in spite of advice to the contrary and has two children. He continues to be refractive to all suggestions as to therapy except when the acute episodes described above occurred.

Roentgenotherapy was completely inadequate, due to patient's lack of cooperation. Through two portals (ant and post) over the stomach a total of but 1,380r was delivered in divided doses, over a period of six months, the patient completing but one full series. The factors were 200 K V, 50 cm T S D, 8 m a, filter 1.8 Mm Cu + 1.0 Mm Al. Operatively, nothing was done to alter the course of the disease by way of radical removal. It is perhaps conceivable to believe that this tumor is so radiosensitive that it is kept at least in abeyance by the small amounts of radiation obtained during repeated gastro-intestinal examinations during the years following his first, and only course of planned radiation.

This is a remarkable case of a male, age 25, living and apparently well five years and 10 months after having been shown to have a reticulum cell lymphosarcoma of the stomach of the Type II, described by Pack and McNeer.

In retrospect, this patient shows a number of the findings that have been considered suggestive of lymphosarcoma—his youth, his ulcer-like symptomatology and operative findings, the tendency to perforate, and the original roentgenologic findings of mucous folds exaggerated to an almost polypoidal degree.

Discussion—Two patients are alive seven, and five years and ten months, respectively, one, with incomplete removal of the lesion and no roentgenotherapy, and the other, with only biopsy and inadequate radiation. This is in distinct contrast to Cases 2 and 3, that had radical excision of the lesion and a greater amount of radiation, only to die from the disease within 10 and 13 months, respectively. A consideration of the other 12 cases of "five-year cure," reveals that a number of these had also received rather unorthodox treatment. Thus, from the analysis of end-results, it is difficult to be dogmatic as to a method of choice in treatment of these lesions as a whole.

It would seem that in the few instances, when the lesion is completely removable, radical surgery offers the best means of cure.

The case for cure by radiation is certainly not as clear-cut from the data assembled. Undoubtedly, remarkable regression of far-advanced lesions often occurs. This is particularly true in more recent years, with improvement in technic. There are at least six cases in the recent literature that have been symptom-free up to two and one-half years, following only roentgenotherapy, and one case (Kaiser, 1934) has gone eight years. However, when apparent cures occur, as in Cases 4 and 5, it becomes difficult to evaluate the absolute

culative results of roentgenotherapy when compared to what might be termed control cases

It would seem that frequently these lesions have a natural history, individual to the particular case and to a degree independent of the method of treatment. At least, until further knowledge is obtained concerning this neoplasm, not only should every attempt be made to treat these lesions, no matter how far advanced, but also histologically exact diagnosis should be obtained more frequently, before pronouncing a gastric neoplasm beyond therapeutic aid.

SUMMARY—(1) One hundred forty-seven cases of primary lymphosarcoma of the stomach have been collected from the literature, and five new cases are added.

(2) They have been analyzed as to age, sex, symptomatology, clinical and laboratory data.

(3) Of the 118 patients operated upon 76 had subtotal gastrectomy, a 50 per cent resectability of the total number of cases (152), with a 15.8 per cent operative mortality.

(4) Thirteen patients are living and well 5 to 22 years after discovery of the lesion.

CONCLUSIONS

(1) Diagnosis is very difficult, only a single case having been correctly diagnosed preoperatively. There are no pathognomonic clinical findings, and, as yet, no typical roentgenographic appearance. Gastrosopy may, in the future, be a valuable diagnostic aid.

(2) A treatment of choice is difficult to evaluate, due to the number of "cures" that have received what is considered inadequate surgical or roentgenotherapy.

(3) Complete surgical removal is of course ideal, but in only a few cases did this appear possible. Radiation alone, particularly with newer technic, has accomplished clinically complete remission of the disease up to eight years even in far-advanced cases.

(4) The course of some of the cases, suggests that there may be definite individual variation in their life history that at times is completely unrelated to the type and extent of therapeutic intervention.

(5) Attention is called to the desirability of establishing a histologic diagnosis of a gastric neoplasm before it is regarded as beyond aid.

The author wishes to express his appreciation to Doctors Whipple, Meleney, Bull and Roberts, for the privilege of having access to the cases operated upon, and to Doctor Pappenheimer, of the Department of Medical Pathology, for permission to use the autopsy material presented in Case 1. The author is particularly indebted to Dr. A. P. Stout, for his kind suggestions and criticisms.

BIBLIOGRAPHY

1893

Kundrat. *Wien klin Wchnschr*, 12, 211-213, 1893.

1897

Paltauf, R. *Ergebn d allg Path u path Anat*, 1897.

1900

Dock, G J A M A , 35, 156, 1900

1901

Fenwick, W S Lancet, 1, 463, 1901

1903

Lecene, L, Petit Rev de Gynecol et de Chir Abd, 66-96, 1903

1905

Ribbert, H Lehrbuch der allgemein Path, Leipzig, 1905

1906

Yates, J L ANNALS OF SURGERY, 44, 599-639, 1906

1908

Buigvad, V These de Paris, 3 vol 20, 401, 1908

1909

Ziesche, H, and Davidsohn, C Mitt a d Grenzgeb d Med u Chir, 20, 3, 1909

1912

Fabian, E Beitr z path Anat u z allg Path, 53, 491-532, 1912

Gosset, L L Presse med, 22, 221-225, 1912

Ruppert, L L Wien klin Wchnsch, 25, 1970-1972, 1912

1913

Flebbe, G Frankfurt Ztschr f Path, 12, 311-336, 1913

1914

Forni, G Riforma med, 30, 624, 1914

Frankel, E Virchows Arch f path Anat, 216, 340-354, 1914

Mallory, F B Principles of Pathological Histology, W B Saunders, 1914

1915

di Giacomia, G Riforma med, 31, 144, 1915

1916

Ghon, A, Roman, B Frankfurt Ztschr f Path, 19, 1-137, 1916

Schlesinger, H Wien klin Wchnsch, 29, 785-791, 1916

Scott, E, and Forman, F Ohio State Med Jour, 12, 323, 1916

1920

Douglas, J ANNALS OF SURGERY, 71, 628-638, 1920

1921

Broders, A, and Mahle, A J Lab and Clin Med, 6, 249-252, 1921

1922

Cutler, E, and Smith, J A Surg Clin N Amer, 1105, August, 1922

1923

*Knazelson, P Wien Arch f inn Med, 7, 117, 1923

Pistocchi, G Policlinico (sez chir), 30, 83-112, February, 1923

Schindler, R Arch Int Med, 32, 637, 1923

1925

Bertolotti, M Minerva Med, 1166, 1925

Meyeringh, H Beitr z klin Chir, 135, 185-202, 1925

*Neuber, E Zentralorg f d ges Chir u ihre Grenzgeb, 31, 309, 1925

*Steindl, H Lancet, 2, 720, 1925

Straus, A, Black, L, Freidman, J, and Hamburger, W Surg Clin N Amer, 977-984, August, 1925

1926

Borrmann, R Hand d spez path Anat u Histol, 4/1, 832-835, 1926

Falta, W Wien klin Wchnsch, 39, 1291, 1926

Holmes, G W, Dresser, R, and Camp, J D Radiology, 7, 44-50, July, 1926

*The asterisk refers to authors presenting cases which have been omitted from statistical consideration, because of insufficient data or lack of definite histologic description

- *Kan, J N Jour Orient Med, 5, 9, 1926
 Minot, G, Isaacs, R J A M A, 86, 1185, 1926
 *Von Redwitz, E Zentralbl f Chir, 53, 2087, 1926
- 1927
 *Froboesse, C Beitr z path Anat u z allg Path, 27, 363-385, 1927
 Gibson, C, and Neuhoof, H ANNALS OF SURGERY, 85, 138-139, 1927
 Hayden, H C, and Apfelbach, C W Arch Path, 4, 743, 1927
 Junghagen, S Acta radio, 8, 317-339, 1927
- 1928
 Ewing, J Neoplastic Diseases, 3d ed, W B Saunders, 1928
 *Freeman, L Colorado Med, 25, 362, 1928
 Jaki, J Deutsch Ztschr f Chir, 210, 381-389, 1928
 *Singer, H A Tr Chicago Path Soc, 13, 453-471, 1928-1931
- 1929
 Kaufmann, J Pathology, vol 1, p 692 (English trans), P Blakiston, 1929
 Leriche, R, Irmann, E Lyon chir, 26, 534-536, 1929
 Sussig, L Pathologica, 25, 1211, 1929
 Turnbull, H M Proc Roy Soc Med, 23, 220-222, 1929
 *Vasilu, T Sang, 3, 257-276, 1929
 Weeden, W M ANNALS OF SURGERY, 90, 247, 1929
- 1930
 Balfour, D C, and McCann, I C Surg, Gynec, and Obst, 50, 948-953, 1930
 D'Aunoy, R, and Zoeller, A Am Jour Surg, 9, 444-464, 1930
 Hintze, A Arch f klin Chir, 162, 345-360, 1930
 Ruggles, H E, and Stone, R S California and West Med, 33, 486-490, July, 1930
- 1931
 Askey, E V, Hall, E M, and Davis, K S West Jour Surg, 39, 839-847, 1931
 Gomez y Gomez Rev cir de Barcelona, 9, 122, 1931
 Haggard, W D Surg, Gynec and Obst, 31, 505-511, 1931
 Leucutia, T Am Jour Med Sci, 188, 612-623, 1931
 Schubach, A Ztschr f Krebsforsch, 33, 126-136, 1931
- 1932
 Brereton, G E Texas State Jour Med, 27, 666, 1932
 Cheever, D ANNALS OF SURGERY, 96, 911-923, 1932
 Hunt, V ANNALS OF SURGERY, 96, 210-214, August, 1932
 Scribner, F P New England Jour Med, 206, 736-737, April, 1932
- 1933
 Cabot Case New England Jour Med, 208, 1167-1169, 1933
 Forbes, R D Surg Clin N Amer, 1361-1363, December, 1933
 Kuss, G Bull et mem Soc nat de chir, 59, 1017-1026, 1933
 Moulouguet, P Ibid, 59, 1026-1027, 1933
 Schlosserer, W Wien klin Wchnschr, 41, 1118-1189, 1933
- 1934
 Cabot Case New England Jour Med, 211, 976-979, 1934
 Cam, Hillemand, and Mezard Arch d mal de l'app digestif, 24, 337-353, 1934
 Gunsett, A, and Oberling, C Bull et mem Soc de radiol med de France, 22, 58-63, 1934
 Kaiser, R Rontgenpraxis, 6, 233-234, 1934
 Matyas, M Arch f klin Chir, 179, 249-255, 1934
 Pattison, A C Arch Surg, 29, 907-922, December, 1934
 Rentschler, C B, and Travis, R C J A M A, 102, 686-688, 1934
 Spitzenberger, O Rontgenpraxis, 6, 667-670, 1934
 Walters, W, and Church, C T Proc Staff Meet Mayo Clin, 9, 182-184, 1934

1935

- *Bastiony, J A, Presno Rev de med y cir de la Habana, 40, 981-990, November, 1935
Clar, K Med Klin, 31, 552-553, April, 1935
Cutler, M Arch Surg, 30, 405-441, 1935
Drane, R Am Jour Roentgenol, 34, 755-758, 1935
Hunt, V, Bennett, L C West Jour Surg, 43, 265-275, May, 1935
Moutier, F Traite de Gastrosopie et de Pathologie Endoscopique et de l'Estomac-Paris-Masson & Cie, 1935
Pack G T, McNeer, G ANNALS OF SURGERY, 101, 1206-1224, May, 1935
*Thomson, T, Howells, L Quart Jour Med, 4, 81-91, January, 1935
Zanetti, S Ann di radiol e fis med, 9, 382-401, August, 1935

1936

- Golden, R Diagnostic Roentgenology, T Nelson & Sons, 1936
Phillips, J R, Kilgore, F H Am Jour Surg, 31, 178-181, January, 1936
*Renshaw, J F J A M A, 107, 426-428, August, 1936

1937

- Collins, E, and Carmody, M Am Jour Digest Dis and Nutrit, 3, 884-888, 1937
Schindler, R Gastroscopy, Univ Chicago Press, 1937

PRIMARY CLOSURE OF PERITONEUM IN ACUTE APPENDICITIS WITH PERFORATION

REPORT OF TWENTY CASES

RICHARD WARREN, M D

BOSTON, MASS

FROM THE SURGICAL CLINIC OF THE PETER BENT BRICHAM HOSPITAL, BOSTON, MASS

DRAINAGE of the peritoneal cavity following appendicectomy for acute appendicitis with perforation is still a problem of universal interest. Statistical analyses are inconclusive, because the absence of a strict classification of cases according to definite criteria establishing the presence of perforation prohibits comparable study in separate reports. Thus Herrick,¹⁷ on the one hand, reports 217 cases with "gangrene or peritonitis" with a mortality of 184 per cent, and Totten,¹⁷ on the other, reports 1,044 cases of "perforation" with a mortality of 26 per cent. Other writers use such terms as "localized peritonitis," "cloudy fluid," and "early diffuse peritonitis." Few state specifically whether there is definite evidence of escape of infectious material into the peritoneal cavity. The following study is an attempt to clarify this problem.

Clinical Evidence—Mikulicz²⁵ was one of the earliest to discuss the problem of peritoneal drainage thoughtfully. Although he had been, for a time, the proponent of "capillary drainage" by large loose gauze packs, in 1881²⁴ he stressed the folly of draining noninfectious conditions. During the same period, many surgeons were following the school of Rehn in practicing evisceration, saline irrigation of the peritoneal cavity, and drainage with soft rubber tubes.

Hotchkiss¹⁹ in this country, in 1906, was one of the first to publish a group of cases in which primary closure was practiced. In the interval 1895 to 1899, he treated 12 cases of peritonitis by gauze packing, with 11 deaths. From 1899 to 1903, he treated 15 similar cases, utilizing small incisions, saline irrigations, and a small cigarette drain, with no deaths. In a third series of 28 cases, 16 were not drained, and only one of the five fatalities occurred in this undrained group.

Bauer,² in 1911, reported a series of 88 cases, with 10 deaths, the peritoneum being closed tightly in all. Wildegans,³⁸ in 1923, speaks of markedly lowering his mortality to 25.5 per cent by nondrainage. This is a high mortality, and evidence again of the incomparability of the groups due to individual variation in selecting cases.

Clairmont and Meyer⁶ report a 4.07 per cent mortality in 172 cases of early perforated appendicitis, which were treated by appendicectomy. Of these, only 24 were drained. They state that their results show more secondary abscesses than in drained cases, but that "by careful observation and opening

of these abscesses at the proper time a larger number of patients will get well by a smoother course, and a larger number of patients will remain permanently in good health than will be the case with other procedures, above all with drainage "

Hall¹⁶ reported 12 cases of perforated appendicitis with "thick pus in the peritoneal cavity," in which the peritoneum was not drained, with no deaths and no pelvic abscesses Shipley and Bailey,³⁴ and Shipley³³ practiced nondrainage in many cases of "early diffuse peritonitis " They had no deaths and one secondary abscess Their criterion of early peritonitis was optical evidence of purulent peritonitis "with the intestines still smooth and glistening "

Marchini²³ found that in cases with local peritonitis, nondrainage resulted in a 17 per cent mortality as compared with 5 per cent in the drained cases In cases with diffuse peritonitis, those without drainage showed 20.6 per cent deaths as against 30.6 per cent in the drained Cafritz,⁷ Kulenkampff,²² and Muelleider²⁷ also report a lower mortality

Colt and Morrison¹⁰ present 105 drained cases of perforated gangrenous appendicitis with six deaths as compared with 28 undrained cases with no deaths These observers, however, do not accept this as final evidence that nondrainage is better, because in their opinion the sickest cases were drained Finally, Gieitz's¹³ experience over 25 years with peritonitis, in which he reports a gross mortality of 83.5 per cent in 1,728 cases with nondrainage, with 172 secondary abscesses, is important It was his influence that inspired the initiation of the Peter Bent Brigham Hospital Series in 1936

The arguments in favor of drainage have been several In the period before asepsis, it was used as a prophylactic measure in the great majority of all celiotomies principally by the early gynecologists, such as Sims, Oldshausen, and Tait To Tait, is ascribed the authorship of the saying "when in doubt drain " Some authors say, that although the drain becomes sealed off from the peritoneal cavity, it acts as an irritating foreign body and reverses the lymph flow away from the diaphragm toward the drainage sinus (Herrick,¹⁷ Totten³⁷) Others feel that the liberation of exudate is important from the point of view of the patient's toxic reaction The chief argument for draining, however, is that the surgeon believes that he has thereby exteriorized the infection He is mentally more at ease, if the thickness of the abdominal wall is not between him and the suppurative focus Bunch and Doughty⁶ report a series of 139 cases of deferred operation in generalized appendiceal peritonitis, with a mortality of 19.3 per cent As a practice, they are in favor of drainage in the cases operated upon Deaver and Pfeiffer¹² and Sworn and Fitzgibbon³⁶ also advocate drainage

Experimental Evidence—There has been considerable experimental work to show that intraperitoneal drains are ineffectual and even harmful Yates'⁴⁰ work, in 1904, which showed that in dogs a drain introduced through an incision in the abdominal wall fails to communicate with the general peritoneal cavity after six hours, is well known Carmine injected into the cavity elsewhere could not be made to pass out through the drain tract, even under

pressure. He found that this six-hour period was shortened in the presence of infection, and that the adhesions formed in infectious cases that were drained were more dense and harbored organisms longer than those in nondrained cases. Rost²⁹ showed that after 12 hours, fluid injected into a drainage tube could no longer be made to pass into the peritoneal cavity but regurgitated around the tube. Buchbinder, Droege Mueller, and Heilman⁵ produced peritonitis experimentally in dogs by creating an isolated open loop of intestine and then attempted to treat the peritonitis surgically. In a series of 33 dogs, they found that if the perforated focus was excised and the peritoneum tightly closed, the mortality was 58 per cent. If the same was done with establishment of drainage, the mortality in 20 dogs was 100 per cent. If no surgical procedure for treatment was performed, the mortality in 31 animals was 90 per cent. The cause of death in the dogs was toxemia from peritonitis. In every case the drains were encapsulated with dense adhesions. Shambaugh and Boggs³⁰ created intraperitoneal drainage tracts in guinea-pigs and dogs in order to test their resistance to infection. They found that the peritoneum and surrounding tissues could not be infected with virulent organisms poured into these tracts after the fourth day. This seemed to indicate that after that time a tract does not communicate with the peritoneal cavity and, therefore, cannot drain it.

MATERIAL CONSIDERED—The present study consists of a comparison of drained and nondrained perforated cases in the five-year period 1933 to 1937, inclusive. To be considered in this series, a case must have satisfied *one* of three criteria. There must have been free organisms in the peritoneal cavity at the time of operation, proven by culture, there must have been an open perforation, described by the operator in his operative notes, or there must have been an open perforation, described by the Pathologic Department in its report. According to these standards, 111 cases were found, 91 drained and 20 not drained. Table I shows the evidence for perforation in each group.

TABLE I

EVIDENCE OF PERFORATION IN 111 CASES OF PERFORATED APPENDICITIS

Nature of Evidence	Localized Abscess 34 Cases		Diffuse 77 Cases	
	With Drain 31 Cases	Primary Closure 3 Cases	With Drain 60 Cases	Primary Closure 17 Cases
<i>B. coli</i> culture	21	2	34	17
Hemolytic Strep. culture	1			
<i>B. proteus</i> culture	1		1	
Nonhemolytic Strep. culture	1	1	1	
<i>B. fecalis alkaligenes</i> culture			1	
<i>Staphylococcus aureus</i> culture			1	
Obvious perforation at operation or in pathology	7		22	2
Ruptured on removal				1

The comparison of the two groups has been pursued with regard to the various complications unfortunately so familiar in cases of appendicitis. The questions of fecal fistula, wound infection, secondary abscess, postoperative reaction, and death have been dealt with separately. Table II shows the results of this investigation.

ANALYSIS OF CASES—(1) *Fecal Fistula* That nondrainage is not a guarantee against fecal fistula, is shown by a recent study by Strauss and Tomarkin³⁵ at Mt. Sinai Hospital in New York. They found 0.5 per cent of fistulae in those cases closed without intraperitoneal drainage. In our 20 cases, however, we have had no fistulae. In 83 cases of our series that were drained, four, or 4.8 per cent, developed fistulae. Our impression is that the drain is the single most important factor in the causation of fistulae.

(2) *Wound Infection*—In spite of every attempt to protect the wound with towels, gauze, or other means, at the time of opening the peritoneum, nearly 100 per cent of infections are to be expected. If the case is drained, very often the intraperitoneal wick will also serve to drain the wound if it is small. In wounds through which an intraperitoneal drain does not pass because nondrainage is being practiced or because a stab wound drain is inserted at a more convenient site, either the wound must be left open down to the fascia or adequate superficial drainage with rubber tissue should be established. In the whole series there is not a case, drained or undrained, whose wound did not show some evidence of infection important enough to be mentioned in the postoperative notes. One case, in which the wound was closed tightly because of lack of clinical evidence of peritonitis, later had a colon bacillus grow on the culture medium and four days postoperatively showed evidence of wound infection.*

(3) *Secondary Abscess*—The incidence of secondary abscesses has been rather carefully gone into. Clauimont and Meyer,⁸ as has been mentioned, found 28 per cent of secondary abscesses. Two-fifths of these required drainage and three-fifths absorbed spontaneously. Gietz¹³ found 172 abscesses in 1,728 cases, or only 10 per cent. In the present series, 17.5 per cent of the drained group and 60 per cent of the undrained group showed some evidence of secondary abscess formation. By abscess is meant any tender mass palpable abdominally or by rectum, not necessarily all requiring drainage. The incidence of abscesses requiring some form of drainage was 8.7 per cent and 20 per cent, respectively. The great majority of these were abscesses in the pouch of Douglas, requiring colpotomy or rectal drainage.

(4) *Postoperative Obstruction*—The problem of postoperative adhesions causing obstruction to the intestines is particularly elusive of satisfactory analysis. Totten has minimized the responsibility of the drain as the cause

* One very early perforated case, with a positive *B. coli* peritoneal culture, which did not develop wound suppuration, has been seen since this series was recorded. This case, however, had unexplained fever and leukocytosis for three days, during the middle of his convalescence. After repeated hot applications, the reaction disappeared, leaving no evidence of inflammation in the wound.

of immediate postoperative obstructive symptoms. Inquiry into the incidence of late obstruction reveals so few individuals in the community at large who fall in the undrained group, that a just comparison cannot be made. None of the 111 cases tabulated could be analyzed from this viewpoint. Accordingly, 25 consecutive cases entering the Peter Bent Brigham Hospital with intestinal obstruction due to postoperative adhesions were studied. Only cases in which it could be definitely ascertained whether the previous operation had been drained or not, were considered. The exact nature of the previous operation and, indeed, often the condition for which it had been performed, could not be determined in many of the cases. It was found that of the 25, 15 had been drained and 10 had not. Our clinical impression is, and the above small series would seem to indicate, that the drain, in clean cases, contributes to a higher incidence of postoperative obstruction. The same cannot definitely be said in the cases of peritonitis with which we are dealing.

TABLE II

COMPARATIVE STATISTICAL STUDY OF 111 CASES OF PERFORATED APPENDICITIS, WITH AND WITHOUT DRAINAGE

	Mortality		Incidence of Secondary Abscess		Fecal Fistula		Wound Infection		Postoperative Reaction		
	Due to All Causes	Due to Peritonitis	Totals	Requiring Drainage	Total Incidence	Total Incidence	Average Maximum Temperature	Average Days Before Temperature Normal	Average Days Before First Bowel Movement		
Undrained	Localized abscess, 3 cases	0	0	0	0	100%	In 3 cases, 101.6° F	In 3 cases, 14.2 days	In 3 cases, 5.0 days		
	Diffuse, 17 cases	3 or 17.6%	1 or 5.8%	9, or 60.0%	3, or 20.0%	0	100%	In 17 cases, 103.0° F	In 17 cases, 15.2 days	In 17 cases, 4.7 days	
Drained	Localized abscess, 31 cases	2, or 6.4%	2, or 6.4%	0	0	—	100%	In 30 cases, 102.1° F	In 24 cases, 11.7 days	In 30 cases, 5.2 days	
	Diffuse, 60 cases	11 or 18.3%	9, or 15.0%	10 or 17.5%	5, or 8.7%	4 or 4.8%	100%	In 50 cases, 102.8° F	In 48 cases, 11.8 days	In 50 cases, 4.4 days	

* Hereafter, the number of cases analyzable is somewhat diminished through deleting those which died too early for consideration.

(5) *Postoperative Reaction*—The best evidence that can be procured from the hospital records as to the extent of the postoperative reaction, we have considered to be the maximum postoperative temperature, the number of days before the temperature returns to a normal level, to stay, and the number of days, postoperatively, before the patient has the first spontaneous bowel movement. It can be seen from Table II that the undrained group shows a slightly greater postoperative reaction according to these standards. The fact that the temperature in the undrained group remains elevated longer, is probably explained by the fact that secondary abscesses were more common.

This period, conceivably, might have been shortened by earlier drainage of the abscesses in some of the cases

(6) *Mortality*—The total mortality is 14.4 per cent. The mortality in the abscess cases is low, 6.4 per cent, while that in the cases without abscess is high, 18.1 per cent. This latter figure is divided about equally between the drained and undrained groups, being 18.3 per cent to 17.6 per cent, respectively. It can be seen, however, that if the cases are considered from the point of view of the cause of death, one, or 5.8 per cent, of the cases without abscess that were undrained died of toxemia or peritonitis. Of the other two, one died of a pulmonary embolus on the fourth day and the other, a case with advanced peritonitis, died on the operating table, probably an "anesthetic death." Of the similar drained group, the same correction brings the mortality down to 15 per cent.

Operative Indications and Technique—At the Peter Bent Brigham Hospital, operation is performed immediately upon all cases of appendicitis seen within the first two days after the onset of symptoms, who are not too sick to stand the procedure. More advanced and longer standing cases, we tend to treat along the lines proposed by Ochsner²⁸. Each case is considered an individual problem, however, without establishing any arbitrary limit of time, such as 48 hours. In cases of abscess, in which the diagnosis is clear, we attempt to perform operation as an elective procedure, preferably after the first week. The patients with abscesses require the closest observation because, although intra-abdominal rupture of the abscess is rare, it has been reported (Bunch and Doughty⁶). The McBurney incision is employed when the diagnosis is clear preoperatively, adding a Rockey extension into the right rectus sheath when necessary. Peritoneal cultures are taken routinely. Silk technique is used throughout, although the peritoneal suture is often changed to catgut. The peritoneum and fascia are closed and the skin and fat left open in all undrained cases in our perforated group. Occasionally, the deeper layers of the fat are approximated with interrupted silk. It may be added that the use of fine silk does not in any way hinder the healing of the wounds in the presence of infection. If any of the ligatures work loose they are carried to the surface by the granulation tissue. The granulation tissue grows rapidly around those that remain fixed (Shambaugh and Dunphy³¹), and small sinuses have not developed, as occasionally happens in wounds where heavy silk is used. Due to the fact that the incision is made in the line of skin elasticity, there is no tendency for the wound edges to separate, and in all cases, except those in which there is a tendency toward keloid formation, an almost hairline scar is left. The immediate cosmetic result is, indeed, remarkably good because of the lack of stitch scars. Postoperatively, the peritonitis cases are put on an Ochsner type of regimen, with a Wangensteen suction attached to a Levin tube in the stomach, until audible peristalsis occurs.

COMMENT—The methods of procedure outlined have impressed us favorably. The patients, on the whole, do not seem as sick in comparison

with the drained cases as the figures might seem to indicate. We believe that an abdominal wound which does not have a drain through its complete thickness is *more comfortable* than one which has. Certainly the lack of a profuse, continual discharge of pus, with a fecal odor, is a help to the morale of the patient and makes the dressings more comfortable.

We do not know what would happen if any of our cases of large collections of pus in abscess cavities were closed primarily. Our opinion is that the abscess wall contains so much necrotic material that external drainage is necessary for eventual discharge of the slough. Of our three "abscess" cases, that were not drained, there were none which showed large pus collections. They were all small, localized collections without thick walls.

It is obvious that the criteria we have used to include cases in this series have their limitations. They indicate nothing as to the amount of peritoneal infection the patient may have at the time operated upon or the extent of his immunity response to it, factors which must always be considered in estimating the prognosis in these cases. We do feel, however, that they are considerably more concrete than other classifications heretofore used, and that the question can only be settled by working along such lines.

Because of the small series of cases, it may be justly argued that the mortality percentage figures are not final. Notwithstanding this, the fact that only one of our 20 patients died of peritonitis is good evidence that nondrainage is not a harmful procedure. Added to this is the fact that the above mentioned patient was one who had had symptoms for three days and had taken cathartics, one whom under ordinary circumstances we should treat without immediate operation.

SUMMARY—(1) Strict criteria for establishing the presence of perforation in cases of appendicitis have been formulated.

(2) Of 111 cases satisfying these criteria over a five-year period, 91 had intraperitoneal drainage and 20 primary peritoneal closure.

(3) A comparison of these two series shows in the undrained group, a lower mortality rate and lessened incidence of fecal fistula, but a higher postoperative reaction and increased incidence of secondary abscess.

CONCLUSION

Primary closure of the peritoneum in perforated appendicitis without abscess is a safe procedure, and warrants further trial in an effort to lower the high mortality rate.

REFERENCES

- ¹ Andrew, I. Giant. The Operation for Acute Appendicitis. Primary Closure of the Abdominal Wound. *Brit. Med. Jour.*, 1, 1172, 1912.
- ² Bauer, F. Zur Behandlung der acuten, freien, eitrigen Peritonitis mit besonderer Rücksicht auf die Frage der Primarnaht. *Arch. f. klin. Chir.*, 96, 938, 1911.
- Brietmann, M. G. Problem of Draining Abdominal Cavity in Cases of General Peritonitis. *ANNALS OF SURGERY*, 101, 662-670, 1935.
- ⁴ Buchbinder, J. R. The Prevention of Peritoneal Adhesions and Encapsulation. *Surg., Gynec. and Obstet.*, 45, 769, 1927.

- ⁷ Buchbinder, J R, Droegemueller, W A, and Heilman, F R Experimental Peritonitis Effect of Drainage Upon Experimental Diffuse Peritonitis Surg, Gynec, and Obstet, **53**, 726, 1931
- ⁸ Bunch, G H, and Doughty, R Treatment of Acute Appendicitis ANNALS OF SURGERY, **106**, 42, 1937
- ⁹ Cafritz, E A Nondrainage of Peritoneal Cavity in Appendiceal Peritonitis J A M A, **108**, 1315, 1937
- ¹⁰ Clairmont, P, and Meyer, M Erfahrungen uber die Behandlung der Appendicitis Acta chir Scandinav, **60**, 55, 1926
- ¹¹ Clairmont, P Zur Anwendung der Laparophoslampe Zentralbl f Chir, **62**, 546, 1935
- ¹² Colt, Z H, and Morrison, M M M An Analysis of the Mortality in Acute Appendicitis with Respect to Drainage and the Variety of Operation Brit Jour Surg, **20**, 197, 1932
- ¹³ Davis, C R Drainage After Operation for Appendicitis ANNALS OF SURGERY, **99**, 637, 1934
- ¹⁴ Deaver, J B, and Pfeiffer, D B Keen's Surgery, **VIII**, p 444
- ¹⁵ Giertz, Knut H Twenty-Five Years Experience in the Treatment of Peritonitis Tr Amer Surg Assn, **54**, 239, 1936
- ¹⁶ Gile, J F, and Bowler, J P Management of Perforated Appendicitis J A M A, **103**, 1750, 1934
- ¹⁷ Guerry, LeG A Study of the Mortality in Appendicitis ANNALS OF SURGERY, **84**, 283, 1926
- ¹⁸ Hall, E P Why Do We Drain Abdominal Cavity in Peritoneal Infection? Texas State Jour Med, **26**, 505, 1930
- ¹⁹ Herrick, Frederick C Acute Appendicitis and Peritonitis Treatment and Mortality Surg, Gynec, and Obstet, **65**, 68, 1937
- ²⁰ Horsley, J S Surgical Drainage from Biologic Point of View J A M A, **74**, 159, 1920
- ²¹ Hotchkiss, L W The Treatment of Diffuse Suppurative Peritonitis Following Appendicitis ANNALS OF SURGERY, **44**, 197, 1906
- ²² Kehl, G W, and Rentschler, C B Acute Appendicitis Complicated by Peritonitis, Immediate and Late Results in 126 Consecutive Cases Am Jour Surg, **29**, 373, 1935
- ²³ Kelley, H A, and Herdon, E The Vermiform Appendix and Its Diseases Saunders & Co, Philadelphia, 1905, p 652
- ²⁴ Kulenkampff, R Gegen das Drain Zentralbl f Chir, **60**, 2252, 1933
- ²⁵ Marchini, F L'abolizione del drenaggio nelle peritoniti purulente circoscritte e diffuse, specialmente da appendicite Arch ital di chir, **28**, 549, 1931
- ²⁶ Mikulicz, I Uber die Anwendung der Antisepsis bei Laparotomien, mit besonderer Rücksicht auf die Drainage der Peritonealhohle Arch f klin Chir, **26**, 111, 1881
- ²⁷ Mikulicz, I Sammlung klin Vort, No **262**, Chirurgie, No **83**, 2307, 1885, Leipzig
- ²⁸ Miller, H C Problem of Draining Peritoneal Cavity Nebraska Med Jour, **15**, 401, 1930
- ²⁹ Muelleder, A Wien med Woch, **1**, 67, 1937, **1**, 98, 1937 Also Int Abst Surg, **65**, 524, 1937
- ³⁰ Ochsner, A J Clinical Surgery Cleveland Press, Chicago, 1902, p 100 *et seq*
- ³¹ Rost, Franz Pathologische Physiologie des Chirurgen Leipzig, 1921, 2 Aufl, p 326
- ³² Shambaugh, P, and Boggs, R Resistance of Drainage Tract to Infection Arch Surg, **30**, 1032, 1935
- ³³ Shambaugh, P, and Dunphy, J E Postoperative Wound Infections and the Use of Silk An Experimental Study Surgery, **1**, 379, 1937

- ³² Shipley, A M , and Bailey, H A Treatment of Appendicitis Complicated by Peritonitis ANNALS OF SURGERY, 96, 537, 1932
- ³³ Shipley, A M Drainage of Peritoneal Cavity and Peritoneal Obstruction (editorial) Surg , Gynec , and Obstet , 60, 1016, 1935
- ³⁴ Shipley, A M Appendicitis with Peritonitis Treatment Without Drainage Southern Surgeon, 3, 308, 1934
- ³⁵ Strauss, A , and Tomarkin, J Acute Appendicitis Surgery, 3, 111, 1938
- ³⁶ Sworn, R R , and Fitzgibbon, G M Analysis of 2,126 Cases of Acute Appendicitis Brit Jour Surg , 19, 410, 1932
- ³⁷ Totten, Harold P ANNALS OF SURGERY, 106, 1035, 1937
- ³⁸ Wildegans, Hans Weitere Mitteilung uber die chirurgische Behandlung der infektiösen diffusen Peritonitis Arch f klin Chir , 127, 239, 1923
- ³⁹ Wilkie, D P D Coll Papers, Dept of Surg Research, Edinburgh, 1935, I Read before clinical congress of Am Coll Surg , Montreal, October, 1926
- ⁴⁰ Yates, J L Experimental Study of Local Effects of Peritoneal Drainage Surg , Gynec , and Obstet , 1, 473, 1905

CONGENITAL CYSTIC KIDNEY TREATED BY URETERAL DRAINAGE¹

GUY L HUNNER, M D

BALTIMORE, MD

FROM THE GYNECOLOGICAL DEPARTMENT OF THE JOHNS HOPKINS UNIVERSITY AND HOSPITAL, BALTIMORE, MD

THERE is a fairly wide consensus of opinion among surgeons that in most cases of congenital cystic kidney surgical intervention is without value

Medical treatment for this condition follows the indications for combating the various forms of renal failure coming under the generic term Bright's disease, and consists of medication, dietetics, hydrotherapy, mental and physical rest, and, when possible, having the patient live in an equable climate

Observations on the treatment of a limited number of these patients during the past 20 years have led to the belief that many of them have bilateral ureteral stricture, which condition augments the renal stasis caused both by the multiple cysts and, in some cases, by lateral pressure of the mass against the upper ureter

If these observations are supported by other investigators, we will have a comparatively simple method, embracing both medicine and surgery, for relieving symptoms, improving the general well-being and prolonging life in these cases where, too often, the outlook has seemed rather hopeless

The discovery that ureteral stricture occurs in many of these cases emphasizes the great importance of an early diagnosis Too often, clinical symptoms of sufficient urgency to drive the patient to a physician do not develop until there has been such complete destruction of the renal tissue that the victim is already in a fatal uremia, or the accompanying vascular changes have led to an intracranial accident Formerly, in the face of such tragedies the physician could assuage the grief of relatives by the observation that, even had an earlier diagnosis of the true condition been made, science held no remedy for a long postponement of the event

What are some of the difficulties preventing an early diagnosis? Because of its rarity, the average practitioner and even the experienced urologist, too often, overlook the significance of signs and symptoms which fairly clamor for a correct diagnosis

The disease is generally conceded to be of congenital origin, it may be transmitted through the male or female, and at times, as Crawford¹ and others have shown, it occurs in many members of the same family Apparently it occurs with equal frequency in the two sexes Braasch,² in reporting on the vast material of the Mayo Clinic, found that in 193 patients with this disease, 98 were females and 95 males These facts should lead us to earlier diagnoses, particularly if there is a suggestive family history of renal disease An unexplained history of recent loss of weight, general malaise, anemia, headache, or gastro-intestinal disturbances should make us suspect a possible

* Read before the Southern Surgical Association, White Sulphur Springs, W Va, December 6, 7, 8, 1938

origin for these symptoms in the urinary tract, and if, in addition to such symptoms, there is a history of backache, pain in the flanks, or bladder disturbances, we are placed on guard to examine most carefully for enlargement or tenderness of the kidneys, and tenderness on palpation over the ureters. These patients sometimes consult the physician with the sole complaint that they have discovered "a lump in the side," but even in such cases, careful questioning elicits the fact that the patient is below par in initiative and endurance, is subject to headache, or has dull discomfort in the lumbar region, various gastro-intestinal symptoms, or disturbances of the bladder function. Any one or more of these symptoms may have been present for so many years, and have so successfully thwarted sporadic efforts at medical relief that the patient finally has taken the fatalistic attitude that he is destined to put up with them, and is jolted into the advisability of another medical consultation only by the discovery of a mass in the side.

With the above history, and an enlargement or abnormal position of one or both kidneys, and the demonstration of tenderness along the urinary tract, omission of a thorough examination of the upper tract is inexcusable. Should the urine show albumin, casts, or other signs of pathology, and should the functional test show a deficiency, or should there be hypertension, or ocular, or other signs of a cardiovascular disturbance, the thorough examination of the upper urinary tract is even more imperative. With the total picture as above presented, one which is so suggestive of chronic Bright's disease, it is fortunate for the patient that, with the most systematic examination of the upper urinary tract, only in rare instances will we be able to demonstrate the condition of bilateral polycystic kidney.

The presence of large bilateral masses in the flanks is the most suggestive physical sign of this disease, but even with the discovery of such masses, the diagnosis is not completed. We need careful roentgenologic studies to differentiate between polycystic disease and bilateral tumor, bilateral hydro- or pyonephrosis, bilateral calculus disease, bilateral renal tuberculosis, and bilateral perinephritis. Since most of these surgical diseases are accompanied by bilateral ureteral stricture, we find in some instances that the bilateral enlargement in the flanks is due to one of these secondary conditions on one side and to another of these conditions on the opposite side.

Usually we gain considerable light on the diagnosis by a plain roentgenogram followed by a series of exposures taken at intervals after the intravenous injection of one of the radiopaque media. However, the intravenous roentgenograms may prove most misleading, and we generally fall back on the retrograde urograms for more accurate data. Since learning of the frequent association of ureteral stricture with most renal diseases needing roentgenologic studies, I have always opposed the retrograde injection of both kidneys at one treatment. Probably in no disease is this more dangerous than in polycystic kidney, and if this condition is suspected, the plain film should be followed by a urogram of one side only with the catheter in its high position. The catheter should be left in the high position long enough to drain off the injected material, and a salt solution irrigation of the pelvis should follow.

before removal of the catheter. If ureteral stricture is present with polycystic disease, ureterograms may be taken with less danger at later sittings, after the narrowed areas have been dilated. Needless to say that the easy and palpably unobstructed introduction of a plain catheter, without a bulb, is not a diagnostic sign of the absence of stricture.

If on palpation of the abdomen, a large mass is discovered in one flank only, this does not exclude the presence of bilateral polycystic kidney. Usually the smaller kidney is palpable and shows signs of some enlargement, and iohentgenograms show suggestive enlargement and deformity of the calices.

As noted above, many of these patients give a history more or less characteristic of Bright's disease and the analyses and other clinical findings usually duplicate those of Bright's disease. Moreover, as in Bright's disease, early death by uremia, or vascular accident, or by intercurrent disease favored by the patient's condition of lowered vitality, is too frequently the experience of victims of bilateral polycystic kidney.

Histologic studies reveal the amazing destruction of the renal tissues induced by the pressure of the myriads of cysts. Just what influence these pressure effects have on the thickening of the walls of the arteries and arterioles within the kidney, and on the narrowing of the lumen of these vessels, and what relationship these phenomena have to the cardiac hypertrophy and hypertension found in such a high percentage of patients with bilateral polycystic disease of the kidney, are questions still under debate and intensive study (Schacht) ³

Frederick C. Heurick⁴ demonstrated graphically, on two freshly removed autopsy specimens of polycystic kidney, the great influence exerted on the renal circulation by the pressure of the distended cysts. "Normal saline was perfused through them at an arterial pressure of 130 Mm of Hg. The average of several observations was 315 cc returning through the vein in five minutes. Without changing the pressure or flow but allowing it to go on continuously, many of the cysts were aspirated with a Record syringe and fine needle, 365 cc of fluid were thus aspirated from the cysts of one kidney. While so doing the manometric pressure fell from 130 to 10 Mm, although the flow was continuous. The pressure was readjusted at the normal. Now, during the same period of five minutes, the volume flow through the kidney was 1965 cc, over five times the volume flowed before aspiration."

In work with ureteral stricture, we not infrequently have patients present histories and clinical findings that place them with a diagnosis of what is commonly termed Bright's disease. The urologist usually sees only those patients in whom such signs and symptoms are accompanied by some so-called surgical complication, such as hydronephrosis, chronic renal infection, calculus disease of the kidney or ureter, the so-called essential hematurias, and various congenital anomalies of the upper urinary tract. Occasionally the patient with a supposedly purely medical nephritis comes under his care. To see the Bright's disease features of these cases, such as repeated uremic convulsions, persistent hypertension, persistent hematuria, and many of the

lesser evils, such as anemia, fever, headache, dizziness, backache, gastrointestinal disturbances, and bladder symptoms, greatly ameliorated or entirely cleared up by the simple expedient of restoring good ureteral drainage, is one of the most striking and satisfactory experiences in medicine.

Such experiences, repeated many times, make one question what rôle the stasis caused by ureteral stricture may have in hastening the destruction of the renal tissue in the kidney already damaged by the pressures incident to polycystic disease. In the past, when polycystic disease has been complicated by infection, calculus, hematuria, *etc.*, we have ascribed these secondary complications to the poor circulation in the renal vessels, and to the stasis of urine due to the deformities of the pelvis and calices. No doubt, the lateral pressure of the large renal mass compressing the upper ureter against the spine also plays an important rôle in causing renal stasis in the occasional case. If, however, we can demonstrate that many of these patients with polycystic disease also have bilateral ureteral stricture, we have at hand a comparatively simple method for the amelioration of many of these secondary complications.

Of far more importance will be the ability to improve the health and prolong the life of many of these victims, particularly when we make early diagnoses, and institute ureteral drainage in time to obviate that portion of the renal destruction that is due to the ureteral stasis. This early institution of good ureteral drainage will serve as a prophylactic against many of the secondary complications, but some of them will occur because of the distortion of the calices by the cysts and the consequent interference with good drainage, and, in the occasional case, because of the ureteral stasis caused by lateral pressure of the renal mass. Of course, in seeking to determine why these complications occur in any kidney, we must keep in mind various contributory factors other than inadequate drainage.

In presenting a series of patients having both polycystic disease and ureteral stricture, it may be well to warn the reader that in many of these cases he need not expect to find striking roentgenologic verification of ureteral stricture. Some urologists still depend on the use of the plain catheter, without bulb, together with the roentgenologic evidence, for a diagnosis of ureteral stricture. I⁵ have shown that with the Kelly method of an cystoscopy one can use a No. 7, 8, or 9 plain catheter, without bulb, and introduce the catheter to the kidney in two-thirds of the cases suffering from the effects of stricture without detecting evidence of narrowing. The smaller catheters, generally used with the Nitze or water-method of cystoscopy, will certainly miss a larger proportion of stricture cases.

For a number of years, it has been my observation that in the patients who come to the urologist because of renal symptoms, and in whom one of the more common congenital defects of the upper tract is found, the patients' symptoms are not due to the particular anomaly *per se*, but to the presence of some form of ureteral obstruction. In, by far, the greater percentage of these patients the obstruction is caused by ureteral stricture, and in a satis-

factory proportion of them the symptoms are improved or entirely cured by the use of the single method of ureteral dilatation

Whether the failure of the ureters associated with congenital defects of the kidney, including polycystic kidney, to show roentgenologic evidence of gross dilatation, in answer to the stasis of stricture, is due to an unusual congenital structure of the entire ureteral wall, is a question for future investigation

For practical, clinical purposes, however, one does find roentgenologic evidence of stricture in most of these cases. In the past many urologists have been missing the finer points of interpretation, and those ureters showing only slight or moderate dilatation, with roentgenologic evidence of one or more areas of filling defect, have been called normal. Unfortunately, they have led many roentgenologists into the same method of interpretation. On withdrawal of the bulbed catheter, the bulb "hangs" in a certain area, or in multiple areas at certain distances above the external urethral orifice. By referring to the ureterogram, usually one can read the filling defects in the otherwise normal-appearing, or only slightly dilated, ureteral lumen, at the areas of narrowing indicated by the bulb test

CASE REPORTS

Case 1—Mrs L. B., age 37, first entered the Medical Dispensary, May 18, 1917, complaining of backache, occasional colicky pains in the right back, and a swelling in the right abdomen, which she had noticed for two years. She had been habitually constipated. The family history did not suggest cardiorenal disease. Large bilateral abdominal masses were discovered and the patient was referred to the cystoscopic department.

Urologic Examination—Investigation revealed a large mass in either flank, interpreted as being large prolapsed, movable kidneys. The urine was normal. The urethra was densely infiltrated and at the first examination a 55 Kelly cystoscope was used. The bladder was normal. A plain catheter without bulb was passed apparently to the right kidney and 40 cc of clear, normal urine were collected in a rapid flow. Four days later, a catheter with a No. 12 Fr. bulb was used, and on withdrawal, the bulb had a firm "hang" in an area about 4 cm. above the bladder. One month later, the patient returned, reporting great relief from the discomfort in the right side. There had been no return of the severe colicky pains. The last menstrual period had been almost free from the severe pains in the right lower pelvis from which she had suffered all during her menstrual life. A No. 12 Fr. bulb was again used for dilatation. The patient returned six months after the first treatment. She reported great improvement in health. There had been occasional slight pain in the right lower quadrant. The right ureter was dilated with a No. 15 Fr. bulb, which "hung" at 9 cm. from the outside. The kidney took 30 cc. to the point of discomfort. Two days later, the left side was investigated, although none of the patient's symptoms had been referred to this side. The catheter was prepared with a No. 12 Fr. wax bulb, and this obstructed completely when the bulb reached the region of the broad ligament. The patient was treated on both sides a few times during the early months of 1918. She constantly reported good health during this time except for occasional slight pain in the region of the right kidney, and this prompted her to return for further treatment.

The patient was not seen again until April, 1928, when she reported very little discomfort during the previous ten years, and she came in this time because of a new complaint, *viz.*, a dragging sense of pain and discomfort low down in the abdomen and low in her back. Four months previously, she had first noticed what she considered

a prolapse of the womb and this was synchronous with the onset of her pain. The symptoms of prolapse and pain were exaggerated when she was on her feet and working but completely relieved by rest in bed. The patient had changed from a condition of emaciation to one of obesity during the previous ten years. Her color was good and she did not appear ill in any way. B P 150/90, Hb 98 per cent, W B C 9,500. Right kidney seemed about 2.5 times its normal size and the left about twice its normal size. During the intervening ten years, we had treated several patients with congenital cystic kidney, and now, for the first time, this diagnosis, which should have been perfectly obvious during her first investigation, was made in this case. The cervix protruded through the vaginal orifice, it was deeply lacerated and there was a polypoid growth, about 6 cm long and quite irregular in outline, protruding from the anterior lip.

A two-hour P S P showed. First hour, 275 cc—30 per cent, second hour, 525 cc—10 per cent.

Right urograms, April 10, 1928, with 24 cc NaI solution. Left urograms, April 12, 1928, with 40 cc NaI solution. After the Cleveland Clinic fire, all early roentgenograms were destroyed including those on this patient.

We discussed the advisability of performing an abdominal hysterectomy, which would enable an examination of the kidneys, but vaginal hysterectomy offered a much safer and less depleting operation for the patient. This was undertaken, April 24, 1928. The adnexa were normal and were left *in situ*, and the vaginal vault was carefully suspended by the various ligaments.

The patient was followed for a year after the hysterectomy, having occasional dilatation of each ureter. The right ureter with one stricture area, 9 cm from the external urethral orifice, was dilated to a No. 16 Fr. The left ureter, with a long, diffuse stricture in the upper ureter and an annular stricture at 6.5 cm from the outside, was dilated to a No. 17 Fr. Final admission. Five years later, August 3, 1934, which was 17 years after her first visit, the patient was brought to the accident room in convulsions. She was admitted to the medical ward. B P 200/90, T 99.8° F, P 116, R 28, Hb 80 per cent, R B C 4,230,000, W B C 20,900, N P N 210 mg per cent. Urine 1,008, large amount of albumin, finely granular casts, a few W B C and R B C. Death, at age 54, occurred on the second day after admission. From the family it was learned that the patient had been failing for about eight months. She complained of being worn out, of gradual loss of vision, of aching and cramps all over the body, and of lumbar pain on both sides. For two months, she had eaten very little. For one month she had been extremely nervous and irritable.

Autopsy—No. 13,787. Congenital polycystic kidneys and liver, mucopurulent bronchitis, emphysema, slight arteriosclerosis.

Gross note on the ureters. "The ureters and pelves are smooth and practically normal in appearance. The pelves are not dilated, perhaps they are a little stretched and elongated. It is difficult to recognize any proper calices. The ureters show no constriction. The bladder seems practically normal." Blocks were not taken from the ureters, and these organs were not saved.

Case 2—Mrs. A. R., age 43, referred January 7, 1928, by Dr. A. A. Pearre, who had studied the patient's condition at the Frederick City Hospital, and concluded that she needed treatment for a pyonephrosis or a possible renal tumor. The patient was a large-framed woman, weighing normally 182 pounds. She had always enjoyed good health and had been a hard-working woman up to three months previously. The family history was negative except that her father died of Bright's disease. Two children living and well. Menopause, normal, one year ago. Three months ago, complained of a sore, dry mouth and since then has complained chiefly of gastro-intestinal symptoms, aversion to food and water, nausea and vomiting, a sense of fulness and pressure across the upper abdomen. About one month ago, had severe pains in both flanks lasting only one day. No frequency of urination. Thinks the volume of urine has been less than normal as

she has been drinking but little water. Some chilly sensations, thinks no fever. Steady loss of weight. The skin and mucous membranes showed a distinct pallor.

Laboratory tests showed the urine to be acid, specific gravity 1.012, albumin 4 plus, no sugar, many pus cells, a few erythrocytes. B P 140/80, Hb 53 per cent, R B C 2,900,000, W B C 14,000, N P N 461, bl sug 117, urea nit 28.28, urea 60.52, uric acid 5.16. Two-hour intramuscular P S P. First hour, 12 per cent, second hour 20 per cent. Daily temperature as high as 102° F.

Physical Examination was without special findings except for the presence of a large mass filling each flank. These were interpreted as enlarged kidneys, they were rather tender on palpation, and the ureters were tender on palpation over the region of the pelvic brim and in the broad ligaments. The left ureter seemed infiltrated in its broad ligament portion, but did not feel like a tuberculous ureter. Careful examination of the urine for tubercle bacilli was negative.

The patient was so ill that we were cautious about active investigations, and, during the month she was in the hospital, we catheterized the right kidney twice, finding it the seat of a colon bacillus pyonephrosis, and the left kidney once, this being the seat of a 40 cc hydronephrosis infected by the *Staphylococcus albus*. With our small bulbs we got fairly definite evidence of ureteral stricture. Ten days after the last ureteral treatment, and after several days of seeming improvement, the patient suddenly developed coma and died within 24 hours.

Autopsy—Church Home No 246. Revealed bilateral congenital cystic kidney, a condition which had not been considered in our clinical investigation, although the urograms showed widespread dilated calices. (Roentgenograms destroyed after the Cleveland Clinic fire.) It had been considered by the staffs at the Frederick Hospital and at the Church Home that the right kidney was decidedly larger than the left. At autopsy the right kidney weighed 720 Gm and the left, which had a complete reduplication of the pelvis and ureter, weighed 1,700 Gm. The ureters were described as appearing normal and were not saved. Other autopsy findings, probably contributory to death, were edema of brain, bilateral, catarrhal, purulent bronchitis, right bronchial pneumonia, and fatty degeneration of liver with focal necrosis.

Case 3—*Synopsis* Interstitial cystitis. Infected hydronephrosis. Bilateral, dilated ureters apparently from peri-ureteritis in bladder walls. Cholelithiasis. Rectocele. Diagnosis of congenital cystic kidney made only after autopsy on Case 2, and comparison of the roentgenograms on Cases 2 and 3. Great improvement in bladder symptoms and in general health after ureteral dilatation. Death three months later.

Mrs. C. G., age 57, was seen in the Johns Hopkins Hospital dispensary, January 21, 1928. When six months pregnant with her only child, 30 years ago, she began having intense bladder symptoms and had to wear a rubber urinal because of incontinence. The child, weighing 15 pounds, was born at eight months. Ever since, there has been much bladder frequency and pain and occasional leakage. One year after the baby's birth, patient was operated upon for ovarian tumor, and for a year bladder irrigations were given, with some improvement. The surgeon reported finding one side of her bladder much thickened. Synchronous with the bladder symptoms, there has been much indigestion, and about twice a year she has an acute right "kidney colic" and indigestion. A plain roentgenogram showed a large gallstone but there was no tenderness in the gallbladder region, and the patient's attacks of indigestion seemed associated with the urinary tract symptoms.

Cystoscopy revealed an apparent widespread interstitial cystitis involving chiefly the left half of the bladder, and in the vertex were tiny lesions suggestive of elusive ulcers. The kidneys showed irregularly dilated pelves and calices, the right side holding 41 cc and the left 16 cc. Both sides were infected. Each ureteral lumen was about 1 cm in diameter from the kidney to the region of the bladder wall, we considered this dilatation as due to the thickened bladder walls rather than to true stricture. The half-hour intramuscular P S P showed

	Ap T	Amt	Per Cent
Right kidney (cath)	7 min	50 cc	5 ?
Left kidney (blad)	10 min	50 cc	5 ?

The outline of the left kidney seemed considerably enlarged and nodular, and we seriously considered the possibility of a renal tumor. While dilating the ureterovesical regions at ten-day intervals, we had the autopsy on Case 2 at the Church Home, and the similarity of the irregular renal pelvis shadows in the two patients drew our attention to the probability that this patient was also a victim of congenital cystic kidney.

The patient's symptoms and the appearance of the bladder steadily improved, until a dilatation of No. 17 Fr. was reached, when the patient was dismissed with advice to her physician in North Carolina that she might later need a series of ureteral treatments, and, in view of her low renal function and absence of gallbladder symptoms, we advised against a gallbladder operation unless it became imperative.

A recent report from a relative says that the patient died about three months after her return home. The immediate cause of death was not mentioned. This report was rather surprising, for the patient was able to board near the hospital and have her treatments in the dispensary, and the apparent gain in well-being and the rapid improvement in her bladder condition seemed to promise a new lease on life. The most adverse clinical finding was the very low functional value, unfortunately, the two-hour test was not repeated after the ureteral dilatations.

Case 4—Mrs. Z. B., age 42, was seen in a state of coma at her home, May 24, 1931. According to her husband she had complained 48 hours previously of a severe headache. The following morning she had seemed well, but that evening she again complained of severe headache and seemed to have become clouded mentally. The next day, the patient had been in coma continuously. When examined, she seemed to be in a quiet sleep. The breathing was heavy but not stertorous. No odor was detected, suggestive of uremia or acidosis. The color was excellent. The pulse was strong and regular but slow, between 50 and 60. Pinching the arms and legs elicited normal reaction. Brief questioning seemed to point to a renal origin for the coma. The patient had a daughter in good health, 19 years of age. Later, there had been two spontaneous abortions at about the third or fourth month, said to have been due to low blood pressure. The tension was said to have altered from time to time between very high and very low levels. Five months previously, there had been an attack similar to the present one, lasting for two days, which was ushered in with severe headache. The patient was sent to the Church Home where the following notes were made: T 101° F, B P 200/85, W B C 14,400, Hb 104, N P N 366 mg per cent, bl sug 266 mg per cent. Eyegrounds showed marked tortuosity of the vessels, no hemorrhage. The patient had not voided for 24 hours and the bladder was catheterized of a small amount of urine which showed Acid, a few R B C, a few granular casts, no bile, sugar +++, albumin ++, acetone +, diacetic acid +. While obtaining the blood chemistry specimen, an intravenous infusion was given of 600 cc of 5 per cent glucose, and on finding the high sugar content of the blood and urine, there were given during the night three doses of insulin, each of 20 units. The following morning the blood chemistry showed N P N 41.4 mg per cent and sugar 122 mg per cent. The patient died 14 hours after admission, and permission for a limited autopsy was obtained.

Autopsy—Through a small midline incision in the upper abdomen, the abdominal and pelvic organs were found to be apparently normal. Adrenals normal on inspection. The kidneys were removed. The left kidney weighed 390 mg, and measured 16x7x5 cm. Entire organ studded with various sized, thin-walled cysts filled with fluid varying in color from clear yellow to opaque and dark brown or black. Largest cyst measured 3.5 cm in diameter. The right kidney weighed 460 mg and measured 16x8x5 cm. The lower pole consisted of one large thin-walled cyst filled with clear fluid and measuring 7 cm in diameter. The remainder of the kidney was studded with irregular small cysts,

apparently less numerous than those in the left kidney No note was made on inspection of the ureters

Case 5—*Synopsis* Bilateral congenital cystic kidney, in which the true diagnosis was delayed for five years after the first hospital admission, and then made only by an exploratory abdominal operation The operation of partial nephrectomy probably resulted in definite benefit to the patient's renal condition, although, apparently, most of the symptoms had been due to the pathologic conditions found in the ureters Symptoms relieved and patient's general health vastly improved by ureteral dilatations, inadequately followed during the past six years Removal of infected tonsils and care of bad teeth in the past year

Mrs O W L, age 20 when I first saw her, in 1932 In March, 1927, at age 15, she was admitted to the Surgical Department because of pain in the right lower quadrant Leukocyte count 12,300 At operation, the appendix contained gas and fecal material and it was considered the site of an acute inflammation The pathologic diagnosis was "chronic appendicitis" Urine was normal at this visit Two years later, the patient entered the cystoscopic dispensary, complaining that she had continued to have attacks of pain in the lower right quadrant similar to those experienced before the appendix operation Abdominal examination revealed enlargement and tenderness of both kidneys and tenderness on palpation over the right ureter at the pelvic brim Urinalysis Pus, and culture of colon bacillus Two-hour P S P First hour, 75 per cent, second hour, 5 per cent Plain roentgenogram negative for stone, night urogram, right kidney much enlarged, pelvis and calices dilated, urine, pus and culture of colon bacillus Diagnosis Infected hydronephrosis, right, cystitis, chronic Treatment Dilatation of right ureter up to No 14 Fr No cultures before patient was dismissed

I saw the patient for the first time, April 5, 1932 She reported good health after her last cystoscopic treatments, in 1929, up until ten days before admission, when she was taken suddenly with a severe pain, this time in the left upper quadrant, radiating downward to the groin With the attacks, there had been frequency and burning on voiding Occasionally there had been some pain in the right lower quadrant "where my appendix was" The patient had married since her last visit, and in January, 1932, there was an early miscarriage without known cause

Physical Examination—Abdomen appears normal On palpation a large mass occupies the left upper quadrant, the lower pole resting on the transumbilical line, and descending freely on inspiration It is slightly tender, and it feels rather more firm than a normal kidney, suggesting a chronic perinephritic mass, but its free mobility is against this view No nodules distinguished Left ureter at the pelvic brim is not tender, but pressure causes desire to void Right kidney easily palpable over its lower third on deep inspiration, seems of about normal size and consistency, freely movable, not tender Right ureter at the pelvic brim not tender, but pressure causes desire to void Appendix region, some gas on pressure, no tenderness Liver border apparently outlined in the gallbladder region, no mass, no tenderness Dragging over sigmoid not tender Genitalia normal size and position, freely movable Left ureter as it crosses through the broad ligament feels like a fine wire about No 8 size One can snap it over the tip of the finger This maneuver is painful and causes desire to void, and reminds patient of a prolapsus sensation she has noticed since her miscarriage four months ago Right ureter not outlined, palpation elicits tenderness, a desire to void, and a sensation of prolapsus of the pelvic organs The house staff had made preliminary studies (Figs 1, 2 and 3) The urine from the left kidney showed many leukocytes, and the culture yielded *Staphylococcus aureus* With the catheter in the left ureter, the half-hour P S P showed

	Ap T	Amt	Per Cent
Left kidney (cath)	3 min	65 cc	30
Right kidney (blad)	3 min	110 cc	30

Two days later with the catheter in the right side, the urine showed a rare leukocyte and negative culture. The half-hour P S P showed

	Ap I	Amt	Per Cent
Right kidney (cath)	5 min	175 cc	40
Left kidney (blad)	14 min	150 cc	25

The delayed appearance time and lower output on the left side may have been due to the temporary reduction in work following edema of the left ureter after the trauma of examination two days previously. A small bulb on the catheter in the examination of each ureter gave a "hang" in the broad ligament region.

Clinical Impressions—"Patient undoubtedly has bilateral ureteral strictures as evidenced by the history during the past three years, and by the present physical findings. While the mass in the flank feels much like an enlarged kidney, or like an infiltration



FIG 1

FIG 2

FIG 3

FIG 1—Case 5. The plain roentgenogram preceding this urogram showed apparent absence of stone, and, as in this film it revealed the tip of the catheter stopped at the level of the third lumbar interspace and the apparent loop of the catheter near the pelvic brim. Note the large dense mass filling the left flank, the large stomach shadow blurring the upper pole of the left kidney, the greater curvature of the stomach crowded upward and to the right by the mass. The inner border of the mass covers the left portion of the lumbar vertebrae II, III and IV. The tip of the catheter stopped apparently by lateral pressure of the mass. No NaI above the catheter tip except in two of the calices. Reflux of NaI into pelvic ureter and bladder.

FIG 2—Case 5. Catheter withdrawn until tip rests at about the pelvic brim, lower half of abdominal ureter filled up to the region where catheter tip was stopped on introduction, reflux of NaI beside pelvic portion of catheter with filling defect in about region of hypogastric node, and another about 2 cm above the ureteral orifice. Reflux to bladder. Filling defect from third lumbar interspace to kidney, with slight shadow of the pelvis and what appear to be clubbed upper and lower calices.

FIG 3—Case 5. Right urogram showing the catheter tip at a point opposite the third lumbar interspace. Note the slight reflux of NaI in the region of the pelvic brim and again in the midportion of the pelvis down to the broad ligament region. Without the bulb, which 'hung' in the broad ligament region, one would have to interpret this roentgenogram as showing a normal ureter. The reading of the pelvis was that of a slight hydronephrosis. Subsequent events, however, reveal that the suggestively splayed character of the calices and the increased shadow of the cortex should have led us to suspect that we were dealing with a congenital cystic kidney.

of the perirenal fat, yet the clinical history, the comparatively free mobility of the mass, and the normal leukocyte count, do not favor the diagnosis of perinephritis. The presence of stricture could account for the patient's recent symptoms. Should have a barium enema and an intravenous series as further aids in the diagnosis' (See Figs 4 and 5).

Preoperative Diagnosis—Multiple bilateral ureteral strictures, bilateral hydronephrosis, tumor in left flank of renal, splenic, pancreatic, or intestinal origin. With the uncertainty of the origin of the tumor mass, we determined upon a left rectus incision, in order to give easy access to either an intra- or extraperitoneal mass.

Operation—April 12, 1932. Dr. Gerald Hurd, assisted by Doctor Hunner. A short

CONGENITAL CYSTIC KIDNEY

exploratory incision along the white line of the left rectus muscle. It was difficult to separate the peritoneum from the deep fascia along the white line, so incision was made through the peritoneum. This revealed a large, multicystic, extraperitoneal mass. Palpation of the right renal region revealed an enlarged nodular mass about twice the volume of a normal kidney. The exploratory incision was enlarged, severing the eleventh and twelfth intercostal nerves and vessels, and the posterior peritoneum was incised and easily stripped forward off the mass. The upper ureter was exposed for a distance of about 8 cm, and except for slight dilatation and thickening of its walls, it appeared normal. The extra-renal portion of the pelvis was rather thick-walled. The upper pole of the kidney was studded with cysts but retained a fairly normal outline and it merged rather abruptly with the much enlarged lower half of the kidney. The half-hour differential P S P had shown about an equal output from each kidney, making it seem extremely unwise to sacrifice the entire kidney. We therefore lifted the lower portion



FIG 4—Case 5. Barium enema. This was taken after passing a No 8 whistle tip radiopaque catheter without bulb well over into the kidney pelvis and combining a urogram with the barium film. This suggests a low cecum the hepatic flexure displaced downward the splenic flexure displaced upward and medially a questionable filling defect at the beginning of the sigmoid. The surprising finding with the better filled renal pelvis is the large dilated set of lower calices which have not shown in previous films, and which apparently are only slightly deformed by pressure of the large mass in the left flank.

FIG 5—Case 5. Intravenous urogram. Note on the left side the spider leg shadows of the lower calices, the absence of any shadow in the left ureter. Note on the right side a good shadow in the upper ureter, and again in the lower pelvic ureter with filling defects in the region of the hypogastric nodes, and again in the broad ligament region about 3 cm above the ureteral orifice. Considerable NaI in bladder in this 30 minute film.

FIG 6—Case 5. February 9, 1938. Compare with Figure 3 taken six years previously. Great increase in size of pelvis probably due to increase in size of cysts and to back pressure by the stricture

of the kidney out of the wound. This mass was irregularly globular and measured 10 to 12 cm in diameter. From this we resected a triangular pyriform mass measuring 6 to 8 cm on each face. The edges of the resected portion were approximated with a No 0 plain catgut in a running lock-stitch suture, one area, about 3 cm long, being left open for temporary drainage. We considered the possibility of this creating a permanent fistula, but it granulated over promptly. After carefully returning the kidney to its normal position, three small cigarette drains were carried down to the open area of the cortex. As in all conservative operations upon the kidney, the foot of the bed was elevated 18 inches for 24 hours, in order to insure a good position for the kidney and upper ureter. The patient was discharged on the twenty-eighth postoperative day. She was not seen again until five years later.

On June 10, 1937, the patient reported having had good health until an attack of influenza the previous winter. Following this, pain gradually developed in both renal

regions and was more severe on the left side. For the previous week the pain had been more severe and was accompanied by nausea. Doctor Everett found that she had bilateral colon bacillus pyelitis, and after several dilatations on either side there was marked relief. At the first visit, a half-hour intravenous P S P yielded

	Ap T	Amt	Per Cent
Left kidney (cath)	10 min	275 cc	30
Right kidney (blad)	10 min	75 cc	15

This seemed to verify the value of our conservative operation on the left side, and to indicate that the right kidney had deteriorated in its working capacity during the preceding five years. This deterioration may chiefly have been due to increase in the size and pressure of the multiple cysts, and, if so, it probably was permanent. On the



FIG 7

FIG 8

FIG 7—Case 5. Note absence of large shadow formerly filling left flank. Again we see the catheter tip obstructed in approximately the same region as in Figure 1. This obstruction may have been caused by a stricture stopping the tip or distal shoulder of the bulb, or a kink stopping the tip. It appears that there is a very narrow area just at the tip and a sharp angulation just above this narrow area. On subsequent treatments we have passed Nos. 10 and 12 bougies, with the sloping end reaching full size 5 cm. back of the tip, entirely over into the kidney. We then passed the No. 9 whistle tip catheter with a No. 12 Fr. bulb over into the kidney and on withdrawal, obtained a strong "hang" at this area, 26 cm. from the external urethral orifice, and "hangs" in the region of the hypogastric nodes and in the broad ligament.

FIG 8—Case 5. November 17, 1938. Shows about the same size pelvis as Figure 6 taken February 9, 1938. The ureterogram shows a sharp angulation opposite the fourth lumbar, where we have frequently met an obstruction to the catheter tip on introduction. However, bulbs up to No. 15 Fr. show "hangs" only in the region of the hypogastric nodes and in the broad ligament where filling defects are seen in the film. The left ureter has given more trouble because of the frequent failure to get through the high stricture (Fig. 7), and a No. 12 Fr. has been the highest dilatation reached.

other hand, the deterioration may have been due, in considerable degree, to the scars of contracting ureteral stricture, and, if so, the reestablishment of good drainage would result in improvement of the P S P output. The patient returned eight months later, February 6, 1938, having been well until February 2, 1938, when she began to have a nagging feeling in the region of the navel, a marked hematuria, and a constant desire to void. The hematuria continued until the day of admission, when severe colicky pains began in the left upper quadrant. The clinical findings were: B P 165/100, Hb 85 per cent, N P N 32, CO₂ 54, two-hour P S P. First half-hour, 200 cc, 40 per cent, second half-hour, 400 cc, 15 per cent, second hour, 720 cc, 12 per cent, total 67 per cent.

I saw the patient, February 9, 1938. After the first day in the hospital there had been some pain after meals but no renal colic. She had not again seen blood in the urine. A catheterized bladder specimen, centrifuged, showed in the h p f, 3 to 4 R B C,

10 to 12 W B C , 10d bacilli, and an occasional hyaline cast The left kidney had been much reduced in size after the operation The lower pole reached the navel line and the kidney felt slightly enlarged, not tender The left ureter pelvic brim region was very tender, and pressure caused a nauseated feeling and a desire to void, and the patient said this was the seat of her chief pain The right kidney was larger than before the operation on the left side, nearly six years previously The lower pole extended slightly below the navel line, and there was slight tenderness

The right ureter (Fig 6) took a No 9 pointed-tip, radiopaque catheter, with spiral wax-tip and small bulb near the tip, encountering three rather dense obstruction areas going in, one of these being near the kidney Free flow, as if some renal retention About 30 cc of urine came out in a steady stream The right kidney specimen reported as containing no R B C , W B C , casts or organisms, but a slant agar culture developed a heavy growth of *B coli* On withdrawal, there was no "hang" of the scant 12 Fr bulb in the area near the kidney, which had firmly obstructed the catheter on entrance, but there were two definite "hangs" in the lower pelvic ureter No scratch marks on tip or bulb The tip had been in originally 35.5 cm above the external urethral orifice Figure 6 shows that the kidney pelvis had more than doubled in size during the six years since Figure 3 was taken Part of this increase in size, no doubt, was due to the general increase in size of the kidney, but some of it may have been due to the stasis caused by the strictures On the following day urograms were obtained on the left side, only one of which is reproduced (Fig 7)

The patient was followed during the summer of 1938, and the right ureter was satisfactorily kept at a dilatation of No 15 Fr

A recent half-hour P S P showed

	Ap. T	Amt	Per Cent
Right kidney (blad)	5 min	120 cc	30
Left kidney (cath)	5 min	75 cc	15

This, compared with the half-hour differential test, made June 10, 1937, seems to show a considerable improvement on the right side since good drainage has been sustained, while the left side, with the difficulties of drainage, has deteriorated

June 10, 1937 The patient reported good health for nearly five years, and then the development of her former symptoms after an attack of influenza This led to the quest for possible foci of infection, and diseased tonsils and teeth were found The teeth were attended to, but the tonsils were not removed until April, 1938 With the more systematic treatment during the past few months, the patient usually reports freedom from all symptoms, and she seems to be leading the normal life of a hard-working housewife

Case 6—*Synopsis* Bilateral congenital cystic kidneys with chief symptoms referred to the gastro-intestinal tract Cholecystectomy, three years previously, without apparent benefit *Preoperative Diagnosis* Tumor of left kidney and possibly of right, bilateral ureteral stricture Occasional ureteral dilatations during the past six years, the patient enjoying comparatively normal health

Mrs M P , age 29, was admitted to the hospital, September 20, 1932, complaining that four months previously she had discovered a mass in the left upper quadrant This was only slightly painful, but it made her nervous and caused pain in the cardiac and left axillary regions Steady loss of weight No hematuria Soon after marriage, 12 years previously, she had an abortion of a one-month pregnancy, and soon had a hysterectomy for pus tubes Three years ago, developed indigestion and mucous colitis for which cholecystectomy was performed, without apparent benefit Last bad attack of colitis about one month ago

Physical Examination revealed a rounded, nodular mass, easily palpable high in the left flank, projecting from beneath the left costal margin This descended freely on deep

breathing. The patient was admitted on the Medical Service, and both Doctors Longcope and Hamman thought there was a tumor of the left kidney, and possibly of the right kidney also. Roentgenograms of the chest were negative. Wassermann negative. B P 116/74, W B C 5,400, Hb 100 per cent. Dr. Gerald Hurd, resident gynecologist, found that there was bilateral ureteral stricture. A half-hour intravenous P S P showed

	Ap T	Amt	Per Cent
Right kidney (cath.)	3 min	75 cc	35
Left kidney (blad.)	3 min	25 cc	25

A few pus cells in the urine from each kidney, cultures negative. Figures 9 and 10 show that the urograms were not particularly helpful in the diagnosis.



FIG 9

FIG 10

FIGS 9 and 10—Case 6. The kidneys show a tendency toward the trifid type the pelves being smaller than normal and some of the calyces possibly showing a slight tendency to dilatation, and, after the findings at operation, one might argue that there is a suggestion of the splayed form of calyx.

Operation—October 6, 1932. Doctor Hurd, assisted by Doctor Hunner. Lumbar, extraperitoneal exploration of left kidney. The kidney was found to be about three times normal size, and filled with numerous small cysts, measuring from 1 to 3 cm in diameter. A small biopsy section was excised, and the renal wound was closed with a mattress suture of plain No. 1 catgut. The lumbar wound was closed in layers, and the foot of the bed was elevated 18 inches for the first 24 hours to favor a good permanent position for the kidney. The patient was discharged in good condition on the sixteenth postoperative day. She was advised to place herself under the care of Dr. Frederick Wright, of Hanover, Pa., for further dilatation of the ureters. She consulted Doctor Wright four months after operation, January 30, 1933, complaining of moderate pain in both renal regions and of frequency of voiding. A catheterized specimen of bladder urine was cloudy, yellow, acid, specific gravity 1,002, sugar none, albumin 2 plus, no acetone or diacetic, a few pus cells. B P 125/70, Hb 79 per cent, R B C 4,288,000, W B C 4,800. Between January and November, 1933, Doctor Wright treated each ureter on four occasions, dilating the strictures up to a No. 14 F. The patient returned five years later, February, 1938, reporting that her health had been good until quite recently when she again began to have aching in the renal regions, frequency of voiding at night, and gastro-intestinal symptoms. The clinical investigation showed urine amber, clear, acid, specific gravity 1,020, albumin one plus, no sugar, acetone or diacetic acid. An occasional pus cell. Blood urea 13.2, N P N 27.4, Hb

90 per cent, R B C 4,568,000, W B C 7,300 Two-hour intravenous P S P First hour, 395 cc 40 per cent second hour, 120 cc, 30 per cent The ureters were again dilated up to No 14 Fr, and a recent report says the patient has gained ten pounds in weight and has had good general health, but recently has had moderate pain at times in the region of the left kidney Doctor Wright plans to have her return for a series of treatments that will carry her ureters to a No 15 or 16 Fr dilatation

Case 7—Figures 11 and 12 are roentgenograms forwarded, February 10, 1933, by Dr Etley P Smith, of Fairmont, W Va, who suspected he was dealing with a case of congenital cystic kidney A Polish coal-miner, age 37, had been sent to the hospital because of hematuria, which followed a blow over the right flank the previous day The family history and the patient's past history were negative, except for a gradual loss of 20 pounds in weight during the past two years

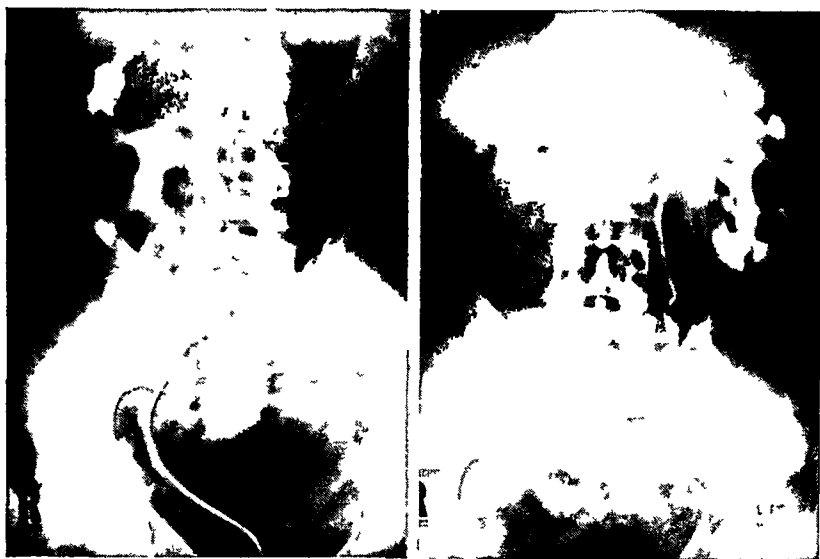


FIG 11

FIG 12

FIG 11—Shows the right ureter crowded over to the midline by the large renal mass narrowing of the upper abdominal ureter (probably by pressure) slight dilatation of the pelvic ureter from the pelvic brim to a point about 4 or 5 cm above the bladder Probably one or more strictured areas in the pelvic ureter

FIG 12—Shows a fine line of ureteral lumen in its vesical 2 cm From this area to the kidney, the left ureteral lumen is slightly dilated except at a point opposite the fourth lumbar interspace Here there is an angulation and possibly a stricture (to be tested with a bulb) Probably definite stricture of vesical portion of left ureter

Physical Examination showed apparent slight anemia, rather flabby musculature, and in the right kidney region a tumor mass, extending down to the pelvic brim, which was movable on respiration, and slightly tender on palpation There were no marks of trauma on the chest or abdominal walls Cystoscopy showed a normal urethra and bladder, and bloody urine spouting from the right ureteral os The urine from the bladder and that from each kidney were essentially alike, showing acid, a heavy trace of albumin, no sugar, W B C, some clumps, R B C (more from right kidney), an occasional hyaline cast, and a culture of a gram-negative bacillus There was no temperature elevation Blood N P N 43 Half-hour P S P, intravenous, showed Right, 12 per cent, left, 20 per cent From a study of the urograms I confirmed the diagnosis of congenital cystic kidney, and added the diagnosis of probable bilateral ureteral stricture

A report from Doctor Smith, November 15, 1937, four and one-half years later, states "During February, March and April of 1933, I dilated the ureters up to No 14 Fr I used bulbed catheters and had considerable difficulty especially on the left side He continued his mining work, and two months after the dilatation was finished he seemed to be in fairly good condition, with the exception that he was having some

pain and a feeling of fulness over the right kidney. His urine was practically clear, but final cultures were not taken. The two enlarged kidneys remained of about the same size. He was definitely improved after the ureteral dilatation, but on attempting to trace him recently one of his friends said he had removed to New York State, and I failed to learn his address."

Case 8—H. I. S., a male child, three weeks old, was referred, July 6, 1934, by Dr. Thomas F. Daniels. The child had been delivered by Dr. William Millea, who reported a long, slow labor due to enlargement of the child's abdomen by bilateral congenital cystic kidneys. The child was large, well nourished, and of good color. The head seemed somewhat enlarged, and the fontanelles were wide, but the child seemed normally alert and bright. The transverse diameter of the upper abdomen was much increased by the presence of a large, solid-feeling, nodular mass occupying the upper portion of each flank. The mass in the left flank seemed somewhat the larger, and its lower pole reached a line halfway between the navel and the symphysis.

Inasmuch as the child seemed in good health, the mother was advised to do nothing unless it developed special symptoms. At six months of age the child was admitted to another hospital with the history that he had been in apparently normal health until the day before admission, when he was suddenly taken with repeated vomiting and diarrhea, the stools soon becoming bloody. These symptoms persisted until death 48 hours after onset of the attack. Autopsy was not obtained. The diagnosis was hydrocephalus, congenital cystic kidneys, intussusception of bowels(?)

Case 9—*Synopsis* Bilateral congenital cystic kidneys. Bilateral ureteral stricture. Small renal calculus, left. Large cyst lower pole right kidney, ruptured and drained spontaneously after first visit. Subacute colon bacillus pyelitis, right, cleared spontaneously after first visit, but was present again on fourth visit, three years later. Chronic pyelitis left kidney, improved, but colon bacillus persists, probably due to presence of calculus. Five hospital visits in four years, resulting in great gain in weight, and practical absence of symptoms.

Mrs. I. S., age 39, seen in consultation with Doctor Everett, September 9, 1934. Complaint: Dysuria, frequency, pain and fulness in right side of abdomen. Para two, 17 and 13 years of age. Labors normal and spontaneous, lacerations with first labor and the first puerperium complicated by fever. G. I. No important symptoms. P. I. During the last two to three months, occasional brief periods of dysuria and frequency. Three weeks ago, during an automobile ride, the patient did not find it convenient to void for about two hours after she first felt the desire. When she did void there was considerable pain, and the next day she had rather marked frequency and burning. She was placed on forced fluids and caprokol, and the bladder symptoms gradually abated somewhat, but a few days later there was pain and discomfort in the right side of the abdomen and slight fever. One week ago, patient was taken to the hospital and cystoscoped and a catheter was left in the right ureter for two days. This catheter is said to have drained pus, and the pain was somewhat relieved. Exploratory operation on the right kidney was advised. Intravenous urograms were taken and are said to have shown active secretion on both sides, also a definite shadow of stone in the left kidney, and a shadow vaguely suggestive of a stone in the right kidney.

Physical Examination—Doctor Everett. The abdomen was found to be soft and flat except for the presence of a large, spherical mass lying in the right upper quadrant, and apparently coming from beneath the costal margin and extending back into the posterior flank and reaching well down to the level of the navel. The left kidney was not felt and tenderness was not elicited in this region. There was slight tenderness on palpation over each pelvic brim region near the spine. Liver and spleen not palpable. Doctor Everett's further studies led him to the conclusion that the patient had bilateral polycystic kidneys, with a subacute colon bacillus pyelitis on the right side and a chronic colon bacillus pyelitis on the left side.

CONGENITAL CYSTIC KIDNEY

With ureteral dilatations at ten-day intervals, accompanied by pelvic lavage with normal salt solution and followed by lavage with a small amount of silver nitrate solution 1:1,000, the patient made steady improvement and was dismissed at the end of two months.

The patient returned one year later in greatly improved general health. She reported occasional slight pain in the region of each kidney, but there were no bladder symptoms, and she had not had fever. All evidence of infection in the right kidney had disappeared but the left kidney still carried a mild colon bacillus infection, probably encouraged by the presence of the small stone trapped in an upper calyx (Fig. 14).

April, 1936. The patient seemed in such excellent condition in every way that cystoscopic examination was not made. The catheterized bladder urine showed only one or two pus cells. A two-hour P.S.P. showed: First half-hour, 400 cc, 20 per cent, second



FIG. 13

FIG. 14

FIG. 13—Shows a small round stone, about 1 cm. in diameter, in one of the upper calices of the left kidney. The right kidney apparently contains a large cyst in its lower pole which displaces the ureteral catheter medianward to the midline of the shadow of the lumbar vertebrae. Doctor Everett thought the pressure of this large cyst on the upper abdominal ureter might have caused the recent acute attack of pyelitis on the right. While both ureters were slightly dilated from the kidney to the broad ligament region, he got no "hang" of a wax bulb on the right side until later treatments had reached a dilatation of 5.6 Mm., when there was a "hang" of the bulb at 27 cm. above the external urethral orifice and another "hang" near the bladder. On the left side the increasing sized bulbs hung at 9 cm. from the outside, and with the 5.6 Mm. bulb there was also a "hang" at 27 cm.

FIG. 14—Shows that the large cyst in the lower pole of the right kidney had drained spontaneously and that the ureter was no longer displaced so far medianward, and the enlarged calices presented a vastly different picture.

half-hour, 350 cc, 10 per cent, second hour, 500 cc, 25 per cent, a total of 1,250 cc, 55 per cent. The patient had gained 25 pounds since her previous visit in September, 1935. There had been no ureteral dilatations since the first visit, in 1934.

April, 1937. Had apparently been in excellent physical condition, but, for about a month, she had been complaining of pain in the left kidney region and had had some light chills and fever, there were no bladder symptoms associated with this attack. She had been feeling better for the two weeks before admission to the hospital. Doctor Everett found, in the left kidney specimen, 15 to 20 W.B.C., and there was still a colon bacillus infection. The half-hour intravenous P.S.P. showed a three-minute appearance time, and a 22 per cent secretion from each kidney. The right kidney had again picked up a mild colon bacillus infection and the urine showed about 5 to 15 W.B.C. Ammonium mandelate was given, which seemed to reduce the amount of pus but did not entirely do away with the colon bacillus, probably because of the stone in the left kidney. Her general condition was so good that Doctor Everett did not attempt further ureteral dilatations.

November, 1938, four years after the first treatments. Patient reported excellent health. B P 138/92, Hb 82 per cent, N P N 28.5. The two-hour intravenous P S P showed a total of 62 per cent, 35 per cent in the first half-hour. A differential half-hour P S P showed 20 per cent from each kidney. Roentgenograms taken at this time are shown in Figures 15 and 16.

Case 10—Synopsis *Bilateral congenital cystic kidney. Bilateral ureteral stricture. Symptoms suggestive of renal disturbance since age 14. Diagnosis of floating right kidney at age 24. Diagnosis of cystic kidneys and ureteral stricture at age 34.*

Miss S. G., age 34, referred, September 12, 1934, by Dr. Herbert Traut, who had made a careful investigation at the New York Hospital, and concluded that the patient had hypertension, reduced renal function, nitrogenous retention, and bilateral hydro-nephrosis, "all probably associated with bilateral ureteral stricture." Some of Doctor Traut's findings were as follows: Urine from bladder a few R B C, Hb 100 per cent,

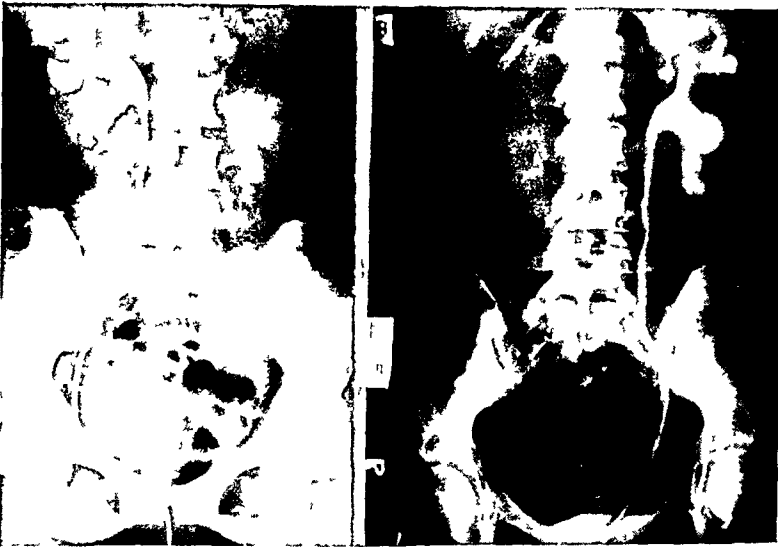


FIG 15

FIG 16

FIG 15—Case 9. Shows a relative narrowing of the right ureter just below the pelvi-ureteral junction and a slight dilatation of the ureter in the broad ligament region down to the ureteral os (compare Fig. 13).

FIG 16—Case 9. Shows the tiny calix with narrow neck depending from the upper group of clubbed calices. Other films have shown that the calculus resides in this tiny calix. With the catheter withdrawn until its tip is just within the ureteral os, there is seen good filling of the upper tract with moderate dilatation of the left ureter and areas of comparative narrowing opposite the third and fourth lumbar interspaces, and a filling defect in the broad ligament region.

W B C 10,250, blood chemistry sugar 77, CO₂ comb power 56, chlorides 469, N P N 45.8. Of two half-hour intravenous P S P's, the second, and higher one, showed

	Ap T	Amt	Per Cent
Right kidney (cath.)	4 min	190 cc	18
Left kidney (blad.)	6 min	120 cc	10

Doctor Traut forwarded urograms of each side to me, from which I concluded that the vertical spread of the pelves, and splayed character of some of the calices, strongly suggested congenital cystic kidney. Some of the points in the patient's history suggesting the probability of renal disease, and especially of ureteral stricture, were as follows: The menstrual periods began at age 18, but for four years before the onset, there had been monthly attacks of extremely severe headaches, dizziness, nausea and vomiting confining the patient in bed three or four days. The menses have been of the 28-day type, with about seven days of free flow. Not incapacitated from work during

this time but always has headache, and pain in the right ovarian region and across the lumbar regions

The first attack, directly pointing to renal trouble, occurred 11 years ago, with a sudden "kidney colic" on the left side accompanied by tenesmus and frequency and the passage of blood. The severe symptoms lasted only about one hour but she was in bed for one week. Ten years ago, had a similar attack of "kidney colic" on the right side, together with hematuria. Was in bed two weeks, and then had two cystoscopic investigations, and was told that the right kidney was enlarged and floating and functioning poorly. The two catheterizations seemed to result in definite relief, and the patient has since worn an abdominal supporter and slept with the foot of her bed elevated eight inches. She has always had some discomfort in the right side since this attack ten years ago, but has not been incapacitated except with an occasional severe attack. One of these occurred eight years ago, when two ureteral catheterizations seemed to result in considerable relief. An attack five years ago was accompanied by hematuria and at that time it was found she had hypertension. Since then she has

FIG 17

FIG 18



FIG 17—Case 10. Note dome like rounding off of the lower calices by a large cyst in lower pole.
FIG 18—Case 10. Note splayed character of calices. Multiple filling defects in left ureter.

followed a low protein diet. The intermittent attacks of severe pain and hematuria without evidence of stone were most suggestive of the presence of ureteral stricture, and even more suggestive of this condition was the fact that the patient had experienced definite improvement in her condition immediately after the use of plain catheters in several investigations. She had been so much relieved by Doctor Traut's recent investigations, using the plain No 7 catheter twice on either side, that she was in no hurry to have me undertake further treatment. For the three or four years preceding her first ureteral investigations, ten years previously, she had had considerable frequency of voiding, always arising four to five times at night. Since these first catheter investigations, the nightly voiding has been only once, and she has not been bothered with diurnal frequency except when she has an occasional "cold."

The patient had severe diphtheria at age 5, and was said to have had a tonsillectomy at that time. She had enlarged cervical nodes as a schoolgirl, but has had no history of tonsillitis. The tonsils are distinctly small and embedded, and, because of the occasional redness occurring about the faucial pillars, I have had them under suspicion as a possible cause of the resistance her ureteral strictures have shown to remain permanently dilated.

In addition to the above symptoms pointing more directly to the urinary tract, her chief complaints recently have been as follows. For perhaps the past six years, she gets up daily with a severe headache, usually occipital, at times frontal. Has worn glasses 20 years, last changed two years ago. Always backache with the menstrual period, and for the past five or six years has usually had a backache when she first arises in the morning. This is always worse in the right upper quadrant, at times some aching in the left upper quadrant. Both the headache and the backache usually disappear after she has been busy a few hours. At times some nausea and dizziness. Digestion good. Bowels regular. At times, when very active, she develops temporary swelling of the feet and ankles.

Physical Examination—The left kidney was found to fill the left upper flank, its lower pole almost reached the transumbilical line, and on deep breathing descended below this level. The right kidney filled the right midflank. Its lower pole rested on a line below the level of the navel, and on deep breathing it descended to a level 5 cm below that of the navel. One could apparently pass the abdominal hand above its upper pole. In its lower third a fairly large nodule projected on its anterior surface, probably causing the dome-like rounding-off of the lower calices, and the median displacement of the right ureter (Fig 17). The patient has four or five dense stricture areas in each ureter (Figs 17 and 18), and, during the past four years, there has been no rest interval between dilatations longer than six months. We have found that, for reasonable comfort, the dilatations must be kept above a No 15 Fr. After a few weeks or months of comparative comfort, the patient again returned with an exaggeration of some of her symptoms, and we began dilatations with bulbs of No 15 Fr size, and on a second pair of treatments we used No 16 Fr and, if the wax bulbs do not mold down, we use a No 17 Fr on the third pair of treatments. If the No 16 Fr bulb molds to a slightly smaller diameter, the subsequent treatments are done with a No 16 Fr bulb until this passes without molding, when we step up to a No 17 Fr. From October 12, 1934, to June 3, 1935, the patient had six pairs of treatments in order to reach a No 17 Fr dilatation. In January, 1935, when we had reached a No 15 Fr dilatation, we took a half-hour intravenous P S P, which showed

	Ap T	Amt	Per Cent
Right kidney (cath)	2 min	50 cc	30
Left kidney (blad)	12 min	30 cc	20

This shows a satisfactory improvement over Doctor Traut's test made five months previously, and registered above. Our two-hour P S P made in January, 1935, showed 30 min, 225 cc, 25 per cent, 60 min, 200 cc, 15 per cent, second hour, 250 cc, 10 per cent.

I think that of all our patients on whom we have had an opportunity to follow the treatments systematically, this patient has had the most regular follow-up and the highest dilatation, but has shown the least satisfactory results. In spite of this, the patient has been able to carry on with regular housekeeping, and as a half-time secretary and stenographer, and I think Dr Traut, who has followed her progress closely, feels, as I do, that without the ureteral dilatations the patient would not be living to-day.

Case 11—Mrs E H, age 54, was admitted to the hospital, May 6, 1935, in apparent extremis, with shortness of breath and general anasarca. One child 35 years of age. Patient first discovered a lump in her right flank soon after this child was born. A lump was discovered in the left flank 11 years ago, soon after an operation for intestinal obstruction. Has worked hard all her life up to two months ago, when the abdominal masses seemed to be getting larger, the edema, which had been intermittent, increased and became constant, and there has been increasing shortness of breath. There have been no bladder symptoms, and patient has not complained of headache or backache. Her mentality, considering her general condition, is remarkably alert. For several months, her appetite has been poor and there has been considerable nausea and vomiting. For two months, the bowels have been loose.

Physical Examination—There seemed to be general edema, most marked over the hands and feet, and about the perineum. The flanks were distended by unusually large masses coming from beneath the costal margin and extending down to the pelvic brim. These were solid-feeling, nodular over the surface, and apparently movable, not tender. Evidence of ascites was not positive. B P 115/80, Hb 68 per cent, W B C 8,000, blood chemistry N P N 156 mg per cent, Wasseimann negative, two-hour P S P 100 cc, color insufficient to be read. May 10, 1935 N P N 208 mg per cent, urine, acid, sugar 0, albumin ++, occasional W B C and R B C, casts 0, diacetic, negative. The patient died on her fourth day in the hospital.

Autopsy—No 14,209. Revealed immense polycystic kidneys, together weighing 14 pounds. There were diffuse sclerosis of the aorta and coronary arteries, cardiac hypertrophy and dilatation, chronic passive congestion of the lungs, cholelithiasis, edema and ascites. There had been no opportunity to examine the ureters clinically. The post-mortem notes on the upper drainage tract were as follows: "The pelves are greatly distorted and open out abruptly into large cyst-like spaces. Near the junction of each pelvis with the ureter, however, the pelvis on each side shows a more or less normal morphology with a pale, smooth, white lining. The pelvis on one side, from the calices at one pole to those on the other, measures 13 cm. It is distorted by pressure of the cysts rather than distended. The ureters are small and thin and seem to be practically normal." Blocks were not taken from the ureters and these organs were not saved.

Case 12—*Synopsis* *Patent ductus arteriosus. Bilateral congenital cystic kidney. Bilateral ureteral stricture. For many years symptoms of headache, backache, gastrointestinal disturbances, mild bladder symptoms, but patient led an active, useful life until the past three years. Family history suggestive of renal disease. Three years of marked improvement after inadequate ureteral dilatation.*

In October, 1935, I received the following letter from Dr. Samuel Weisman, of Parsons, W. Va.: "Mrs. V. T., of this city, has consulted me complaining of general malaise and lassitude for the past three years. Her past history reveals that she was admitted to a local hospital about two years ago for a cardiac lesion which has since improved. Her general condition, however, has remained the same, and, on examination, I find that she has a large, irregularly shaped mass in each side of the abdomen. On careful palpation the surfaces of these masses appear to be studded with variously shaped nodules. The mass on the left seems to be the larger one. Both move with respiration. They are not tender. Unfortunately, there is no way of telling whether these masses were present on her previous hospital sojourn, as there was no record of any abdominal examination, and the patient does not recall any discussion of these masses."

The patient was admitted to the hospital, October 23, 1935, at which time we added the notes summarized in the synopsis recorded above. The suggestive family history was as follows: Patient's mother and an older brother and sister all have died of apoplexy during the past five years. A younger sister is now having occasional dilatation of ureteral stricture by Dr. H. D. Furniss, of New York City. (Seeing this last statement while compiling this paper, I wrote Dr. Furniss, asking whether this younger sister showed evidences of congenital cystic kidney. He replied that the patient had been referred to him soon after she had been operated upon for chronic appendicitis and gallstones. The patient's former surgeon reported that he had palpated the right kidney during the operation and found it to be one and one-half times the normal size, but that it seemed smooth in contour. Doctor Furniss kindly sent me prints of his urograms, and while these are not at all positive, they are suggestive of congenital cystic kidneys.)

Physical Examination—In addition to verifying Doctor Weisman's description of the conditions found in the abdomen, we could palpate the edge of a large, hard spleen. There had been no history of typhoid or malaria. B P 160/90, Hb 60 per cent, W B C 7,500, two-hour P S P 30 min, 550 cc, 28 per cent, first hour, 250 cc, 15 per cent,

second hour, 300 cc, 10 per cent, total 1,100 cc, 53 per cent NPN 32 mg per cent, sugar 110, Wassermann negative Catheterized bladder urine Specific gravity 1.013, acid, trace albumin, culture negative Dr Benjamin Baker interpreted the heart condition as due to a patent ductus arteriosus and probable mild aortic coarctation

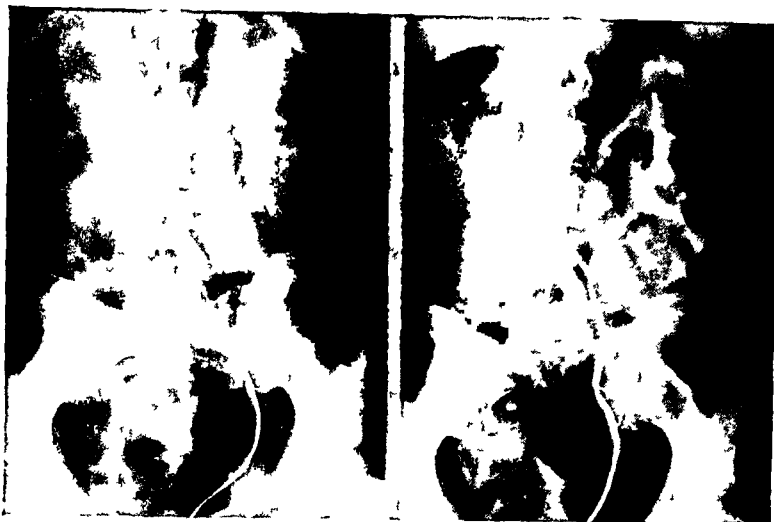


FIG 19

FIG 20

FIG 19—Shows tip of radiopaque catheter at about brim of the pelvis after its partial withdrawal from the previous high position. In other words, it had been stopped permanently at a point about opposite the fourth lumbar transverse process where one sees a narrow area and a lateral deviation of the ureter. Patient complained of colicky pain referred to the bladder when only 45 cc of NaI had been injected by 18 inch gravity pressure. The original film shows reflux of NaI below the catheter tip down to an area a few centimeters below the pelvic brim, and another slight dilatation of the lumen in the region of the broad ligament.

Note the failure of the NaI solution to reach beyond an apparent funnel like pelvic ureteral junction. This failure to fill the upper abdominal ureter may have been due to spasm to narrow areas in the upper ureter or to lateral pressure by the large mass. The No. 11 Fr bulb had a definite 'hang' at 12 cm from the external urethra and again in the broad ligament region. Note rudimentary 12th ribs, dense shadow filling left flank, and shadow of descending colon displaced laterally.

FIG 20—Shows a urogram taken ten days after Figure 19. The No. 10 bougie with 5 cm tapering tip enters the left side with considerable obstruction in the upper ureter, the patient complaining unusually much of pain in the upper flank and extending down to the groin and to the knee. A No. 8 whistle tip catheter with a No. 10 Fr bulb placed near the tip then meets an obstruction to the tip or the distal shoulder of the bulb when the tip has entered 27 cm above the external urethra. Anuria for about one minute, then the catheter is drawn down about 13 cm until the bulb 'hangs' in an area about 11 cm from the outside. Then practically normal spurts of a slightly bloody urine. The urogram shows slight dilatation of the ureter from the position of the bulb in the broad ligament to a relative narrowing opposite the fourth lumbar vertebra. Just above this apparent filling defect there is a double shadow suggesting extravasation, but this irregular shadow is probably due to tetany of the ileopsoas muscle, for we see above a fairly good filling of the upper ureter and the pelvis and calices suggesting the picture of a congenital cystic kidney. The unusual amount of pain experienced when the No. 10 bougie suddenly passed an obstruction in the upper ureter, suggested a splitting of the walls of a high stricture area, and the patient had an unusual amount of pain and soreness in the left flank for five days after this examination, although the temperature rose only slightly above 99° F. These facts later led me to believe that the urogram shows an extravasation rather than a blurring of the ureteral shadow by spastic contractions of the ileopsoas. (In general when gradually dilating high stricture I believe it safer to depend on the use of dilating bougies, but experience has taught that one can split a stricture area with the dilating bougie and extreme care must be exercised even when using the bougie with its filiform tip reaching full size 5 cm back of the tip.) Ten days later a No. 11 bougie was passed 35 cm without undue resistance and without subsequent reaction.

Cystoscopic Examination revealed a much narrowed, infiltrated urethra, the bladder mucosa normal, the trigonum congested, right ureteral orifice very small, secreting freely, left orifice in a red area, not seen, found with curved metal searcher, very small. A No. 9 bougie with 5 cm graduated tip enters left side 35 cm, considerable obstruction throughout its passage, and definite drag on withdrawal. Bleeding from orifice and free spurts of urine. No spurts seen before dilating. Then a No. 7 whistle-tip radiopaque catheter carrying wax bulb of size No. 11 Fr placed near the tip. The catheter obstructs permanently in about the midportion of the abdominal ureter. Anuria about one minute, then the catheter withdrawn about 10 cm, when a normal flow begins in peristaltic waves (Fig 19).

In spite of our urging that she remain until we could establish a No 14 or 15 Fr dilatation, the patient became homesick and left after three weeks of hospital treatment. The hemoglobin had risen from 60 to 70 per cent and the patient appeared greatly improved.

A recent letter from her, three years after what we considered inadequate ureteral treatment, shows that she has gone far beyond our expectations in her recovery from a condition of practically bed-ridden invalidism.

Case 13—*Synopsis* Preoperative diagnosis: Tumor of left kidney. Ureteral stricture multiple, left. Hydronephrosis slight bilateral. Spina bifida occulta. Operation—Exploratory celiotomy. Lysis of omental adhesions. Operative pathology: Congenital cystic kidney, bilateral omental adhesions (former operations), multiple cysts of liver. Postoperative treatment: Intermittent ureteral dilatations up to a 5 Mm (No 15 Fr) for two years following operation. Marked improvement in general health, but after a few weeks of overexertion sudden death due to cerebral hemorrhage.



FIG 21

FIG 22

FIG 21—Shows a urogram taken during patient's second treatment of the right side. The Nos 10 and 12 bougies were first passed meeting resistance in the lower ureter and dragging considerably on withdrawal. The No 8 pointed tip radiopaque catheter with spiral wire tip and No 13 Fr bulb near the tip, then passed with definite obstruction to the bulb in the lower ureter. Free flow slightly blood-tinged urine. Right kidney takes slowly 10 cc nupercaine without discomfort. This retained until patient reached roentgenologist. The low position of a large right kidney is clearly seen. The radiopaque catheter is well over in a lower median calix. Instillation of 18 cc NaI. Right pelvis moderately dilated. Calices considerably dilated and spread out in a manner characteristic of congenital cystic kidney. Normal funnel-like pelvic ureteral opening. Reflux of NaI beside catheter to an area opposite the fourth lumbar vertebra. Moderate deviation of catheter toward spine.

FIG 22—Shows catheter withdrawn until the bulb "hangs" at 13 cm from external urethra. Slight dilatation of upper ureter down to this area. Slight reflux of NaI around catheter in mid-pelvic portion of ureter. The 4.3 Mm (No 13 Fr) bulb "hung" at 13 cm and in one lower area.

Mrs. E. P., age 38, was admitted to the hospital, January 9, 1936. Married 17 years, para two, ages 12 and eight years. Stormy pregnancies, "due to nephritis and hypertension." Six years ago a therapeutic abortion, followed one year later by abdominal operation for sterilization. Eleven years ago, first abdominal operation for Gilliam suspension and appendectomy. Before operation at that time, the right kidney was palpable and the urine was negative. For many years had had hypertension, the systolic pressure being 230 at one time. There has been considerable headache and much mental depression. Edema of the ankles if active on her feet. Has always had rather severe dysmenorrhea and pain in the lumbar region during menses, these symptoms not improving after childbearing. Much gastro-intestinal disturbance, often accompanied by a "dollar spot" of rather severe pain located just to the left of the navel. For two years past, patient has noticed that, following the evening meal, the left side of the abdomen was markedly fuller than the right. Two months before admission, the

patient had a severe left renal colic. The pain in the left costovertebral angle remained steady and constant for two days, and on the third day there was marked hematuria.

Physical Examination was unimportant except as relating to the urinary tract. The left kidney seemed to be prolapsed and considerably enlarged. The lower pole reached a line about 5 cm below the transumbilical line. The upper pole apparently could be outlined by deep bimanual palpation high up beneath the costal margin. The main portion of the renal mass seemed to lie beneath the rectus muscle and the median border lay along the midline. There was some tenderness on palpation of the upper third of the mass. The right kidney apparently could be completely outlined. It seemed



FIG 23



FIG 24

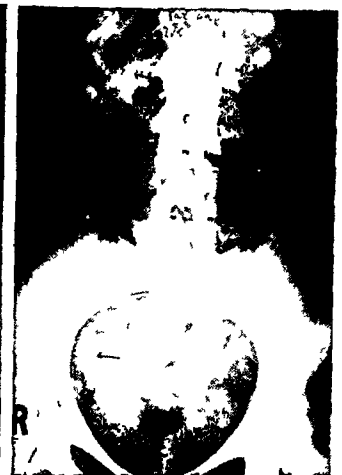


FIG 25

FIG 23—Shows the catheter tip apparently in a lower calyx. Upper middle and lower calices somewhat dilated and clubbed. Renal cortex shadow apparently continuous downward into the shadow of a large mass filling the left flank and reaching to the crest of the ilium. About 4 cm below the lower calyx is an oval shadow, about 3x13 Mm resting on the midportion of the mass shadow in the flank. No evidence of NaI connecting the lower calyx with the shadow lying over the mass. No definite shadow of the renal pelvis, but the calyx shadows suggest a trifid type of kidney, in which case one would expect the pelvis to be small. No reflux beside the catheter down the ureter. The right lower flank appears filled by a dense shadow, and riding over this is the gas shadow of the hepatic flexure and of the descending limb of a prolapsed transverse colon. The ascending limb of the transverse colon on the left is apparently crowded toward the spine by the mass in the left flank.

FIG 24—Is taken with the catheter withdrawn until the bulb "hangs" in an area at about the region of the hypogastric node and the tip is resting at about the pelvic brim. There is slight reflux of the NaI to the level of the bulb and the abdominal spindle is of about normal diameter. Beside the fourth lumbar vertebra and the lower edge of the third, the ureteral lumen is very narrow. The upper end of the ureter widens slightly to merge with the pelvic ureteral junction, which is indistinctly outlined. On withdrawal of the catheter we noted that "it came down about five centimeters and then the bulb (serial No. 11 Fr) 'hung' fairly firmly over a long diffuse area in about the midabdominal ureter."

FIG 25—Intravenous urogram. The ten minute exposure shows active functions in both kidneys; the normal sized bladder being well outlined. In the left flank, there is seen the group of three clubbed calyx cups, apparently representing the upper and middle calices, and at some distance below these an indistinct shadow representing a pair of dilated lower calyx cups. Still lower and to the left of the third lumbar vertebra is a small shadow, probably representing the lowermost separate calyx seen in Fig 24, and in one of the intravenous films this was seen to be connected with the pelvis by a thin spider leg primary calyx. The right pelvis with its moderately dilated calices is better outlined. The No. 9 bulb had no "hang" on the first investigation of the right side, but with the definite demonstration of multiple stricture in the left ureter, we felt that the presence of moderate hydronephrosis on the right side would, with the use of a larger bulb, be found to be due to stricture. Note spina bifida occulta of the fifth lumbar vertebra.

of normal or slightly enlarged size, in second degree descensus, rather firm, and somewhat tender over its upper third. The ureters were tender on palpation at the pelvic brim and in the broad ligament regions. B P 154/92, Hb 64 per cent, WBC 6,240, blood sugar 69 mg per 100 cc, NPN 45.4 mg per 100 cc. Urine, acid, specific gravity 1.018, faint trace albumin, two WBC, no RBC, no casts. Two-hour PSP. First hour, 250 cc, 40 per cent, second hour, 500 cc, 15 per cent.

Cystoscopic Examination—Urethra generally infiltrated, dilates with some difficulty to No. 9 Fr, No. 8 Kelly cystoscope, bladder normal, trigonum and ureteral orifice

CONGENITAL CYSTIC KIDNEY

regions moderately red and vascular. The left ureter was catheterized with a No 7 whistle-tip radiopaque catheter prepared with a scant 3.6 Mm (No 11 Fr) bulb near the tip. There was obstruction to the tip, or bulb, in the broad ligament region and again near the kidney. A free flow of clear looking urine which showed microscopically a few epithelial cells, and proved negative on a slant agar culture. A half-hour intravenous P S P showed

	Ap T	Amt	Per Cent
Left kidney (cath)	5 min	55 cc	8
Right kidney (blad)	5 min	105 cc	22

Operation—January 16, 1936 *Tentative Diagnosis* Tumor of the left kidney. Because of the uncertainty of the diagnosis, an exploratory incision was made through the left rectus muscle. This revealed a large polycystic left kidney. On exploring the right kidney it was found to be slightly larger than normal, and nodular with multiple cysts. Several nodules were felt on the inferior surface of the liver near the cystic duct and one nodule on the lower edge of the liver appeared like a retention cyst. The cecum was considerably dilated. The transverse colon was prolapsed and on exploring the pelvis a dense band of adhesions was found attached to the previously suspended uterus. This band spread out fan-wise to form a very small omentum. It was ligated and severed from the uterus, thus freeing the omentum and transverse colon. On more careful exploration of the left kidney, the upper pole, while still retaining a fairly normal outline, was found to contain many fairly large cysts. It was, therefore, decided not to resect the larger lower pole, and the abdomen was closed, in the hope that the patient might be benefited by later ureteral dilatations. The patient developed a post-operative pyelitis on the left side, but the fever subsided completely on the sixth day. Before operation, the urine from the bladder and from each kidney had been negative to culture. Before the patient was discharged, each ureter was dilated on two occasions up to a No 12 Fr bulb. Multiple stricture existed on either side, the highest stricture on the left being 25 cm and on the right 23 cm from the external urethral orifice. On each dilatation, colon bacilli were grown from the left kidney and culture from the right kidney was negative.

The patient was discharged 43 days after operation. Ten weeks later she reported that she developed pain on the right side together with fever, and a few weeks later had a similar attack on the left side. There had been a gain of six pounds in weight. The old pain in the left kidney region was present at times, but there had been no severe attacks except the one accompanied by fever. She had been on her feet a great deal for the past month and frequently developed swelling of the ankles.

Dilatations were carried on for two years at intervals of one to six months, finally reaching a No 15 Fr on each side. On March 10, 1937, 15 months after operation, her report of progress contained the estimate "I feel 1,000 per cent better than for several years before operation." Her gain in weight had been from 117 to 130 pounds. The menstrual periods, for many years accompanied with severe pelvic and lumbar pains, and not relieved after childbearing, now seldom gave trouble. Her last treatment was in June, 1937.

Early in January, 1938, two years after operation, the patient reported that she was having a good deal of headache, backache, gastro-intestinal distress and swelling of the ankles. She lived with her two daughters in a third-floor flat, and in making merry during the holidays there had been much extra stair-climbing and other household duties. I advised that she spend as much time as possible during the succeeding week resting in bed, and then if not greatly improved to return for further treatments. A week later a cerebral hemorrhage occurred, followed by death in a local hospital two days later. I had arranged for an autopsy to include the entire urinary tract, but the

assistant-resident pathologist reported that the ureters "appeared normal" so were not removed

Case 14—*Synopsis* History of attacks of pain in left flank for nine years Bilateral congenital cystic kidney Bilateral ureteral structure Calculus left ureter Good health to date 20 months after treatment

Mrs M M, age 34, was admitted to the hospital, January 10, 1937 One child, age 4, living and well Menstrual history normal P I Patient has had three attacks of pain in the left side, the first, nine years ago, the second, three months ago, the third three weeks ago Each attack came on suddenly, with severe pain beginning in the left lower abdomen and extending upward and back to the posterior flank The pain has not extended downward to the perineum or thigh, but with each attack there has been a constant desire to void No hematuria seen Each attack has persisted for several



FIG 26

FIG 27

FIG 26—Case 14 Right urogram showing bifid type of kidney with pelvis smaller than normal but with dilated primary calices and rather characteristic splayed type of secondary calices Note calculus in left ureter opposite spine of ischium

FIG 27—Case 14 Bifid type of left pelvis which is smaller than normal Dilated splayed secondary calices Instillation of 15 cc of NaI reminded patient of her former attacks of pain This roentgenogram was taken with head of the table lowered 45° because the film immediately preceding this showed no filling of the abdominal portion of the ureter—still absence of filling, possibly due to lateral pressure of the large renal mass Shadow of stone not seen, probably covered by the bladder shadow

hours until relieved by hypodermics or oral medication Has had nausea and vomiting with each attack Has always enjoyed a good appetite, but for the past two years there has been considerable eructation of gas and a sense of fulness across the upper abdomen

Physical Examination—The abdomen is flat and appears normal, but palpation reveals a large movable mass in either flank The mass in the left flank descends to a point about 5 cm below the transumbilical line, and the inner border of its lower pole reaches almost to the midline The upper pole cannot be identified beneath the costal border The surface seems smooth, and there is slight tenderness on bimanual pressure The mass in the right flank is slightly smaller, its lower pole descending to a line 2 cm below the transumbilical line, and its median border reaches almost to the midline at a point 2 cm above the navel The upper pole cannot be outlined The ureteral regions are tender at the pelvic brim No desire to void on pressure The outlet and pelvic organs seem normal The left ureter can be palpated in the broad ligament region, and on high palpation one apparently outlines a stone about the size of a navy bean The right ureter is not palpable Pressure over each ureter causes an urgent desire to void Urine negative Hb 96 per cent, WBC 8,200, Wassermann negative, NPN

29, two-hour P S P First half-hour, 175 cc, 10 per cent, second half-hour, 150 cc, 15 per cent, second hour, 500 cc, 20 per cent, total 45 per cent

Cystoscopic Examination—The urethra was infiltrated and was dilated to a No 9 Hegar with difficulty. The bladder, trigonum and ureteral orifice regions appeared normal. Free spurting of urine from both sides. On the first attempt to dilate the left ureter, we could not pass even a fine whalebone filiform farther than 3 to 4 cm. Seeing the patient at monthly intervals for three times, we finally dilated each side to a No 14 Fr. On March 16, 1937, after passing dilating bougies to a No 14 Fr on the left side, we introduced the alligator forceps and grasped the stone, situated about 5 cm above the bladder, and removed it. Just before this operation the two-hour P S P showed: First half-hour, 200 cc, 35 per cent, second half-hour, 240 cc, 15 per cent, second hour, 205 cc, 10 per cent, total 60 per cent.

On writing this patient a year later to remind her of the importance of a follow-up study to make certain her ureters were draining freely, she replied that she was expecting her second child within ten days, and that she had had no headache and no backache since her treatments and her physician assured her there had not been a trace of albumin during the pregnancy. Writing her during the preparation of this paper, nearly two years after the treatment, elicits the reply: "I hope to get down in May or June. I had my baby last March, a boy, and he is the picture of health. I had a very easy delivery and have felt fine since I came home from the hospital. My urine was normal at that time, and I have not been examined since. I have had no further pain in either side, and no bladder symptoms of any kind."

SUMMARY OF RESULTS—In the 14 cases reported, the diagnosis of congenital cystic kidney was first made at operation in Cases 5, 6 and 13, all of these having had the probable diagnosis of renal tumor.

The diagnosis was first made by autopsy on Cases 2 and 4. Autopsy was obtained on three others, Cases 1, 11 and 13, thus confirming the diagnosis already made.

In Case 8, the three weeks old boy, the diagnosis had been made by the obstetrician and the pediatrician on the presence of extremely large nodular masses in either flank.

The diagnosis was made solely on the presence of bilateral abdominal masses and the characteristic urograms in Cases 3, 7, 9, 10, 12 and 14.

Opportunity to investigate for the presence of ureteral stricture was obtained in 11 cases (in all except Cases 4, 8 and 11) and stricture was diagnosed in ten cases. In another patient (Case 3) with interstitial cystitis, we found dilatation of the ureters which we attributed to the infiltration of the bladder walls. It may be of significance that in this case the ureters were more widely dilated than in any other member of the group.

Of the ten cases receiving either adequate or inadequate dilatation of the ureters, the following is a brief summary.

Case 1 died 17 years after dilatation was begun, and after 16 years of fairly good health.

Case 3. Interstitial ureterovesical thickening. One month of dilatations. Marked improvement in health. Death three months later.

Cases 5 and 6. Each in remarkably good health six years, to date.

Case 7. Continued work as a miner for about one year, then moved to another state and observation ceased.

Case 9 Excellent health to date, four years

Case 10 Fair health to date, four years

Case 12 Such dense strictures that treatment for three weeks carried dilations to only No 13 Fr on right side and No 11 Fr on left side Practically bed-ridden for three years before treatment, and, in view of her congenital heart lesion, has been much too active in the three years since

Case 13 Fairly good health for two years, then death from cerebral hemorrhage

Case 14 Uneventful delivery of child one year after treatment and in excellent health to date, eight months after delivery

In seeking to estimate the value of this method of treatment, fortunately we are not entirely dependent on the patient's subjective response, but have, in addition, the objective evidence furnished by our repeated clinical studies. If there is marked anemia, this usually improves rapidly with the patient's improvement in general health. If there is hypertension, we observe a variation in response, as we do in dealing with ureteral stricture in general. In some patients with hypertension, the restoration of better renal drainage through the method of dilating ureteral stricture results in a decided and permanent decrease of the tension as long as the better ureteral drainage is maintained. In others, there is little or no decrease in the hypertension. If the patient with cystic kidney has blood nitrogen retention, this usually improves promptly on the establishment of better renal drainage. If the renal function, as indicated by the two-hour intravenous P S P, is subnormal, it usually increases as the ureteral drainage improves. If a pyelitis exists, it may clear up completely with no other treatment than the establishment of better drainage. Naturally, in dealing with these extremely malformed pelvises, we are surprised when the ureteral dilatation, in a case with infection, results in a urine negative to culture, but in those instances in which the infection fails to clear completely, there is often restoration to such good drainage that the patient has no symptoms directly attributable to the continued presence of bacteria.

CONCLUSIONS

(1) Medical and hygienic treatment is helpful in many cases in relieving symptoms more or less characteristic of Bright's disease.

(2) Surgery offers the only hope of relief when certain secondary emergency complications arise. Inasmuch as the cystic disease is practically always bilateral, necessary surgery should aim at the conservation of all renal tissue that promises to recover. If preliminary examination reveals signs of malignant tumor or tuberculosis of one kidney, one should hesitate about operation unless careful tests show that the remaining kidney has fair promise of *sustaining life*.

(3) Evidence has been presented suggesting that many of these patients have bilateral ureteral stricture, and that in such cases, through simple ureteral drainage, we may obtain more prompt and more prolonged relief than pre-

viously has been thought possible. This calls for the earliest possible diagnosis in all suspected cases, and if stricture be present, we should establish the level of dilatation at which the individual patient seems to do best, and follow the patient at intervals, for years if necessary, to keep the ureters at their optimum of drainage.

(4) While this disease is of congenital origin, we know that some of its victims, without treatment, live to a ripe old age in the enjoyment of apparently good physical and mental health, and sometimes a diagnosis is made only at the autopsy table. Such facts should deter us from overenthusiastic claims concerning the value of any line of treatment. However, one cannot study the case histories presented above without concluding that the ureteral drainage methods have been of decided benefit in those cases where given adequate trial.

REFERENCES

- ¹ Crawford, R. H. Polycystic Kidney. *Surg., Gynec. and Obstet.*, **36**, 185, 1923.
- ² Braasch, Wm. F., and Schacht, F. W. Pathologic and Clinical Data Concerning Polycystic Kidney. *Trans. Amer. Assoc. Genito-Urinary Surgeons*, **25**, 71, 1933.
- ³ Schacht, Frederick W. Hypertension in Cases of Congenital Polycystic Kidney. *Arch. Int. Med.*, **47**, 500, 1931.
- ⁴ Herrick, Frederick C. Some Observations on Polycystic Kidney. *Ohio State Med. Jour.*, February, 1921.
- ⁵ Hunner, Guy L. *Practice of Surgery*, Lewis, **8**, Chap. XI.

DISCUSSION—DR. R. H. CRAWFORD (Rutherfordton, N. C.) I am happy to obtain from Doctor Hunner, help in this type of case. Eighteen years ago we began the study of a family—intelligent people who could give an excellent history concerning themselves. Apparently the condition followed through four generations. The first two, we had to take from the history given us. In the remaining two generations we saw the majority of the patients.

In the fourth generation there were ten children. One died of typhoid at 13 years of age, but I saw and examined the remaining nine. They all had tumors—I thought one had escaped, but he now has two tumor masses meeting in the midline. Each of them has lived to between 30 and 45 years of age. A very interesting part of the study, which is still in progress, and I hope to be able to give it in detail eventually, is the fifth generation. Some of the children have congenital cystic kidneys. In the third generation, hematuria seemed to be the principal symptom, although toward the end they had a typical Bright's disease. The striking thing is that these large tumors were present without much discomfort. One patient had carried-on for a number of years as a teacher in a boys' school. He died at about the age of 40. Another, a dentist, had two tumors, and kept up his work until his death at 45. I think he lived longer than any of the nine. I hope to complete the study this year if we can get the children worked-up.

EARLY RECOGNITION OF SHOCK AND ITS DIFFERENTIATION FROM HEMORRHAGE

VIRGIL H. MOON

PHILADELPHIA, PA.

A REVIEW of hypotheses concerning shock, of the facts which invalidate many of them, of the associated physiologic disturbances, and of recent interpretations resulting from a revision of experimental methods, will not be attempted here. Those interested in the author's analysis of the origin, mechanism and pathology of shock are referred to recent publications.¹

A combination of evidence, from the fields of capillary physiology and of experimental pathology, indicates that diverse injurious agents and conditions exert harmful effects upon the capillaries, that any type of injury to capillaries causes the endothelium to become abnormally permeable to blood plasma, that dilatation of capillaries and venules in extensive visceral areas lowers the *effective* blood volume, and leakage of plasma decreases the *actual* blood volume, that these effects produce a disparity between the volume of blood and the volume-capacity of the vascular system, which disparity manifests itself in the syndrome of shock, and that hemoconcentration occurs regularly when this type of circulatory disturbance is developing.

Hemoconcentration—The fact that hemoconcentration occurs when shock from various causes is developing has been known for many years. The earliest observations on this feature were, apparently, made in clinical studies on patients suffering from extensive burns of the skin. Baraduc² (1863) noted in such cases that the blood was dark, thick and that it failed to clot. He believed this change was related to the mechanism by which death occurred, that the thick, viscid blood could not circulate through the minute vessels and that this resulted in death by circulatory failure. Tappener³ (1881) reported erythrocytic counts, ranging from 7,810,000 to 8,960,000 in from six to 17 hours after burns, in four cases which resulted fatally. Wilms⁴ (1901) confirmed the previous observations and recorded cell counts ranging from 6,500,000 to 8,200,000 in six persons severely burned. Locke⁵ (1902) reported blood counts in ten such cases. The highest count in four nonfatal cases was 7,266,000, while in five of the six fatal cases the erythrocytes were above 9,000,000. He recorded that the blood was dark and thick. Becky and Schmitz,⁶ Underhill, *et al*,⁷ Simonait,⁸ Moon,⁹ Wilson, *et al*,¹⁰ Harkins¹¹ and others have confirmed that marked hemoconcentration occurs immediately after severe superficial burns of the skin.

Underhill and his associates reported blood studies in 20 cases of severe superficial burns. Marked hemoconcentration was found in each instance, as indicated by hemoglobin percentages ranging from 114 to 226 per cent. The higher concentrations were found in the more severe cases. The condition

was associated with a decreased return of blood from systemic areas and with decreased volume output of the heart. This resulted in systemic anoxia, lowered metabolic processes, low arterial pressure and final suspension of vital activities. He believed that hemoconcentration is a prime factor in the development of shock from burns. He stated that the degree of concentration is an index of the patient's condition, that neither man nor animals can long survive hemoconcentration of 140 per cent, and that the condition becomes precarious at 125 per cent.

Sherrington and Copeman¹² (1893) noted an increase in the specific gravity of the blood of animals after abdominal operations. They suggested a relationship between this feature and surgical shock. Cobbett¹³ (1897) described a series of experiments in which the specific gravity of the blood was noted at intervals after manipulation of the intestines of dogs. The data included a continuous record of arterial pressures. For a time the specific gravity was unchanged, but as edema and serious effusions developed, the specific gravity rose steadily and the blood became thickened so that it flowed with difficulty. For some hours after the specific gravity began to rise, the arterial pressure showed little or no sign of falling. When, at last, the blood pressure began to decline, it fell rapidly and death occurred soon. Cobbett noted three stages of effects in such experiments:

(1) Fluid was lost from the injured tissue, but the blood was unaffected because of fluid absorbed from other tissues.

(2) As the compensatory absorption of fluid became insufficient, the density of the blood gradually increased and signs of failing circulation began to appear, but the blood pressure remained unchanged.

(3) A rapid decline in blood pressure ending in death.

He concluded that circulatory failure after severe abdominal operations, in peritonitis and after burns, is accompanied by similar alterations in the blood.

Vale¹⁴ (1904) recorded the specific gravity of the blood and tissues in experimental shock in animals and in human cases of shock from various causes. In experimental shock the specific gravity was increased and that of the tissues decreased, which indicated an increased fluid content of the tissues and a consequent inspissation of the blood. Shock in human cases, resulting from trauma, burns, peritoneal inflammation and from other causes, was accompanied by an increased specific gravity of the blood. An exception to this was seen when the condition had been complicated by considerable hemorrhage. The specific gravity returned to normal when recovery from shock occurred. Vale suggested that the observed phenomena resulted from damage to capillary walls. He was the first author to suggest that variations in specific gravity of the blood present a practical means for distinguishing between shock and hemorrhage.

Crile¹⁵ (1909) recorded that in experimental shock the red cells are increased in number, but after hemorrhage their number per unit volume is decreased. Henderson¹⁶ (1910) found the blood abnormally concentrated in

shock, and attributed this to leakage of plasma into the tissues Mann¹⁷ (1914) and many others have confirmed these observations, but none of these authors suggested the practical use of this test clinically

Cannon, Fraser and Hooper¹⁸ made cell counts on the blood of seriously wounded soldiers. They found red cell counts ranging from 6,000,000 in mild shock to above 9,000,000 in severe shock. The hemoconcentration was progressive and tended to be proportional to the degree of shock. Conversely, a decreased number of erythrocytes was found after hemorrhage and also in the blood of those who had served as donors for transfusions. Bayliss and Cannon¹⁹ found corresponding hemoconcentration in experimental shock in cats. Bazett²⁰ found red cell counts of great value as indicating whether shock or hemorrhage was present and in determining the condition of the patient and the operative risk. In Robertson's²¹ experience patients suffering from shock are to be distinguished from cases of hemorrhage or from hemorrhage plus shock by the presence of a high hemoglobin reading in the former.

The above findings were confirmed by Keith,²² who showed that a marked decrease in the total volume of blood is an outstanding feature of shock. This is due to a decrease in the plasma volume and is accompanied by hemoconcentration. He concluded that one prominent factor was that the normal processes of blood dilution fail to operate. In moderate shock the blood cannot absorb fluid from the tissues nor from the gastro-intestinal tract, but the vascular walls are able to retain fluid if supplied in suitable form. In severe shock the vascular walls are unable to retain colloids or even whole blood. Fluids leak out into the tissues almost as fast as injected. Treatment in this class of cases was entirely ineffective.

Bainbridge and Bullen²³ found the hemoglobin content reduced after hemorrhage and increased during shock. They advise this as a practical means for differentiation of those conditions. They observed that the system is able to compensate for loss of blood by hemorrhage but that in shock this mechanism failed to operate.

There is agreement among investigators that decreased total volume and volume-flow of blood are essential features in the mechanism of shock. There has been disagreement concerning the origin of these features. A threatened disparity, between the blood volume and the volume-capacity of the vascular system, is compensated for a time by physiologic means. Activity of the sympatho-adrenal system results in maximal systemic vasoconstriction, thereby reducing the volume-capacity. Organs such as the spleen discharge their reserve of blood into the circulation. Fluid is absorbed from tissues into the blood, thereby increasing its volume. Let it be emphasized here that this mechanism of absorption depends directly upon the normal state of the capillary endothelium. Capillary walls so atonic and permeable that they allow plasma and cells to transude into the tissue spaces, are incapacitated for the function of absorption. The development of capillary atony deranges the mechanism of "water balance" and throws out of gear the machinery for compensating a

decreasing blood volume So long as the mechanism of compensation is effective, there is no ominous decline in the arterial blood pressure

Compensation and Arterial Pressure—A decline in blood pressure has been regarded as the characteristic sign of shock, and few have realized that this is a sign, not of the developmental stage, but of circulatory decompensation When the arterial pressure sinks below 80 Mm Hg—"the critical level"—the end is imminent

Many authors have noted that a *rise* in blood pressure follows trauma of various kinds used in producing shock experimentally We have noted this feature after injecting small amounts of tissue extracts intravenously The injection of large doses caused the pressure to decline Similar observations were made after implanting muscle pulp intraperitoneally (Chart 2) The increased arterial pressure under such conditions indicates effective compensation which may be followed by a decline, indicating decompensation This view is supported by clinical experience Gray and Parsons²⁴ stated that "a low blood pressure is not an essential accompaniment of the clinical picture, for the classical symptoms of shock occur while the blood pressure is at its highest recorded point "

Cope²⁵ stated that a fall in blood pressure is not the earliest nor the truest indication of shock, that no appreciable decline in pressure may occur until more than one-fourth of the total blood volume is lost, and that the pressure may be well maintained with a much smaller blood volume He cited instances in which a late stage of shock was present while the blood pressure was well maintained He stated that many cases of serious shock will pass unrecognized if low blood pressure is used as the chief or the sole criterion

Freeman, Shaw and Snyder²⁶ devised a method for determining the volume-flow of blood in human beings Their results indicated that a progressive reduction of the volume-flow was present during the development of surgical shock In some instances the volume-flow was reduced almost to zero before the blood pressure gave any indication that shock was present They concluded that variations of volume-flow of blood are more accurate indications of the presence and of the degree of shock than are variations in arterial pressure However, no simple practical method has been devised for determining the volume-flow of blood clinically

A Clinical Test for Shock—Kennedy and I²⁷ confirmed the finding that hemoconcentration develops before pressure changes occur both in experimental shock and in human cases Later we reported on the practical application of this test to clinical use Our results showed that hemoconcentration occurs early, that it is proportional to the degree of the condition and that it is a clinical test of high practical value in detecting this type of circulatory deficiency, in estimating its severity and in differentiating it from hemorrhage

My associates and I have produced shock experimentally by various means in more than 300 animals These included 147 dogs, 98 guinea-pigs and smaller numbers of cats, rats rabbits and monkeys Hemoconcentration occurred regularly without exception in each animal and species This devel-

oped early, before other signs of shock appeared, and the concentration of the blood progressed in degree proportional to the apparent illness of the animal. When recovery followed, the blood returned to its normal corpuscular composition. When death resulted, the postmortem findings indicated capillary atony in extensive visceral areas. This evidence included marked dilatation and engorgement of capillaries and venules with evident stasis of blood in them, ecchymoses, edema of soft tissues, and effusions in the serous cavities. The edema fluid and effusions were shown to have a high specific gravity and protein content, approximating that of the blood plasma.

Hemoconcentration may be shown either by hematocrit readings, by an increase in the specific gravity, by hemoglobin determination or by erythrocytic counts. Our experience indicates that the latter is more satisfactory as an index than either of the others. The erythrocytes sometimes increase in size by swelling. In such a case the hematocrit reading is not an accurate index of hemoconcentration. The curves of successive hemoglobin readings are more irregular and present more inexplicable variations than those of the red cell counts.

Accurate specific gravity determinations are difficult to make as clinical tests, though the method of Hammeischlag is simple and sufficiently accurate if carefully done. This consists in mixing chloroform with either xylol or benzene in such proportion that the specific gravity of the mixture ranges between 1.060 and 1.070 as shown by an ordinary urinometer. A drop of fresh blood is then placed in the mixture, using care to avoid including a bubble of air. If the drop sinks, a small amount of chloroform is added to increase the specific gravity of the mixture. If the drop of blood floats, xylol is added. When the mixture is adjusted so that the drop of blood remains suspended, neither rising nor sinking, it has the same approximate specific gravity as the fluid. This is then determined by a specific gravity spindle.

Variations in the specific gravity of the blood occur in a much narrower range than variations in counts of red cells. For example, before operation or injury the specific gravity may be 1.060 and the red count 4,900,000. When shock has developed, examination of the blood may show 1.075 specific gravity and 8,000,000 red cells. In this instance, the variation in the specific gravity was only 0.015 while that of the red cell count was 3,100,000. The index providing the widest range minimizes the variations due to technique.

We have found that hemoconcentration develops gradually after severe trauma, operations, intestinal obstructions and burns, but that it results immediately after the injection of bile peptone, histamine, emetine and other substances which cause damage to endothelium. A rise from 5,000,000 to 6,000,000 red cells represents a concentration of 20 per cent. Such a finding indicates that the total blood-volume has been reduced about 10 per cent, and the plasma-volume about 20 per cent. A hemoconcentration of 20 per cent is ominous, for it indicates that the mechanism of shock is in operation even though no decline in arterial pressure or other evidence of circulatory deficiency is shown. Hemoconcentration of 40 per cent is a grave sign and is soon

followed by other evidences of circulatory disturbance. When the systolic pressure sinks below 70 or 80 Mm Hg the hemoconcentration may be anywhere between 40 and 60 per cent. Concentration of 80 per cent has been recorded frequently in the terminal stages of shock.

Differentiation Between Shock and Hemorrhage—Hemorrhage and shock are often confused because of the similarity in their clinical signs. They may be differentiated readily by observations on the concentration of the blood. Loss of blood by hemorrhage results in dilution of the blood because fluid is absorbed rapidly from the tissues to restore the blood to its normal volume. The hemodilution is proportional to the amount of blood lost. This fact has been known for many years, and is illustrated by the following experiment.

The specific gravity, hemoglobin content and red cell count of a dog weighing 10.5 Kg were carefully determined. Measured quantities of blood were then withdrawn at intervals, from a vein in the leg. The results are shown in Table I.

TABLE I

ALTERATIONS IN SPECIFIC GRAVITY, HEMOGLOBIN, AND RED BLOOD CELLS AFTER WITHDRAWAL OF 100 CC OF BLOOD

	Time	Sp Gr	Hb	Red Cells	Bled
3-15	11 00 A M	1 056	98	5,400,000	100 cc
	3 00 P M	1 055	97	5,320,000	100 cc
	5 00 P M	1 055	95	5,300,000	
3-16	10 00 A M	1 055	80	5,400,000	100 cc
	11 30 A M	1 050	75	4,910,000	100 cc
	1 00 P M	1 047	57	4,400,000	100 cc
	2 30 P M	1 042	60	3,890,000	100 cc
	4 15 P M	1 037	49	2,420,000	100 cc
3-17	9 00 A M	1 032	36	1,380,000	
	9 30 A M				400 cc (death)

In each instance the blood examinations were made *before* the withdrawal of the volume of blood shown. It will be seen that a loss of 700 cc of blood within 36 hours was sustained by a dog below average size. This reduced the hemoglobin to 36 per cent and the specific gravity to 1.032. At this time the dog showed no evidence of illness. It was active, normally playful, and probably would have recovered. A further loss of 400 cc of blood, however, caused death.

Chart 1 shows diagrammatically the composition of normal blood in the first column. The second column shows the composition when hemoconcentration of 40 per cent is present. About 7 cc of this concentrated blood (third column) contains the same volume of corpuscles as is present in 10 cc of normal blood. This results from the loss of 30 cc of plasma from each 10 cc of blood. In other words, the plasma-volume has been reduced by 50 per cent, and total blood-volume by 30 per cent. The last column (right) shows the composition of blood after a hemorrhage which has reduced the hemoglobin and red cells to 40 per cent of the normal.

Simple examinations of the blood will usually differentiate between circulatory deficiency resulting from hemorrhage and that resulting from shock. In the former the blood is *below*, in the latter *above*, its normal or previous concentration. It may happen that the effects of hemorrhage are combined with the mechanism of shock. Such a combination is indicated by a *less marked* change in concentration. Therefore, when circulatory deficiency is developing, and yet the blood is only slightly above or below the concentration shown prior to operation, there is evidence that shock is combined with the effects of hemorrhage.

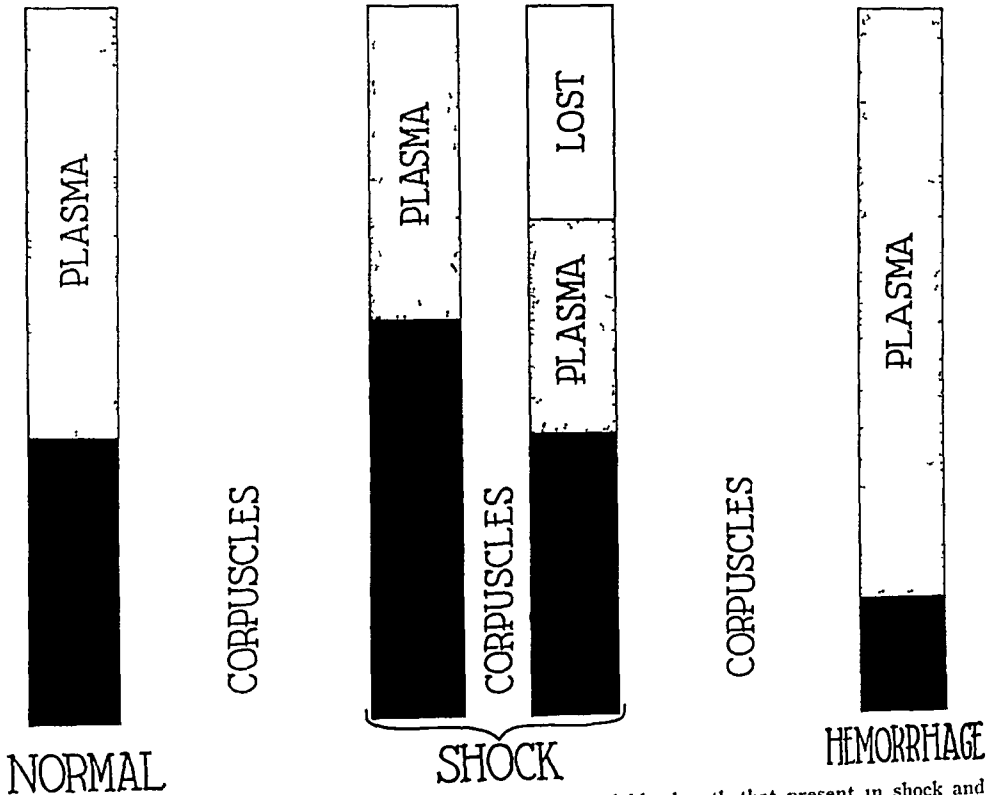


CHART 1—Showing a volumetric comparison of normal blood with that present in shock and that resulting from hemorrhage. If normal blood (first column) becomes concentrated 40 per cent, it will have the composition shown in the second column. Seven cubic centimeters of such concentrated blood will contain the same volume of corpuscles (third column) as 10 cc of the normal blood, 3 cc having been lost. In shock with hemoconcentration of 40 per cent the normal blood has lost 30 per cent of its total volume and 50 per cent of its plasma volume. The fourth column illustrates the hemodilution which occurs when the corpuscles have been reduced by hemorrhages, to 40 per cent of the normal.

Experimental and Clinical Shock—It has been shown⁹ that the shock syndrome occurs clinically in many conditions other than after trauma or extensive operative procedures or after burns. My colleagues and I have produced shock experimentally by various methods which duplicated closely the conditions of its clinical occurrence. Surgeons are most concerned with shock resulting from extensive traumatic injury or from surgical intervention. The following method closely approximates the conditions resulting from extensive injury to muscles.

A quantity of muscle was excised aseptically from a freshly killed normal dog. This was finely ground up in a meat chopper under aseptic precautions.

and was then suspended in saline solution. Varying quantities of this preparation were introduced into the peritoneal cavities of normal dogs under light ether anesthesia. Records were made of the pulse rate, respirations, temperature, hemoglobin content and red cell count three times each day before and after this procedure.

When doses of 5 Gm or more per kilogram of body weight were used, illness developed within two or three hours. Thirst was evident, but vomit-

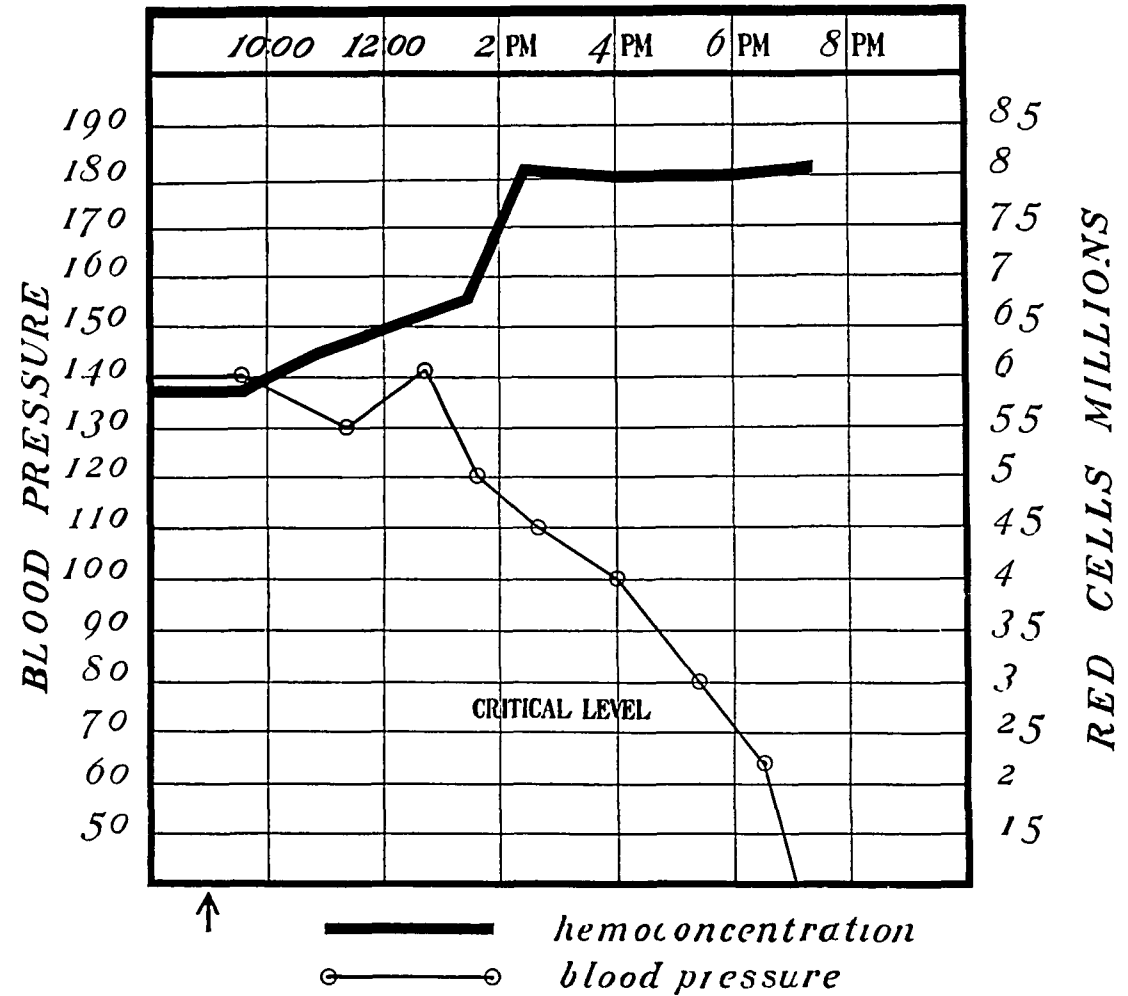


CHART 2—Showing the curves of hemoconcentration and blood pressure as shock developed after placing muscle substance in a dog's peritoneal cavity (arrow). Blood pressure is shown at the left and red cell counts in millions at the right. Clock time is shown at the top. It is seen that hemoconcentration developed immediately, reaching 15 per cent four hours later, at which time the blood pressure was above 140 Mm Hg. The blood reached its maximum concentration four hours before the blood pressure declined to the critical level, 70 to 80 Mm Hg.

ing followed when fluids were taken. The vomitus contained bile, mucus and flecks of blood. The urine was scanty and often contained blood. Diarrhea frequently developed, and the feces showed mucus and bloody fluid. Hemoconcentration sometimes developed within an hour and it occurred regularly before the arterial blood pressure began to decline. The concentration was progressive and its degree was proportionate to the apparent illness of the animal. A condition of collapse, relaxation and stupor preceded death.

Smaller doses of muscle substance produced the same signs of illness, but less rapid in development and in degree. Death did not occur so early. Re-

covery often occurred after doses of 3 Gm or less per kilogram of body weight

Shock was produced by this method in each of 56 dogs. Many of the results of those studies have been reported elsewhere. In one group of experiments the dogs were maintained under light ether anesthesia through a tracheal tube and a continuous kymographic record of arterial blood pressure was made for comparison with the curve of the hemoconcentration. In such instances shock developed more rapidly because of the contributory effect of anesthesia. The following experiment is typical of this group

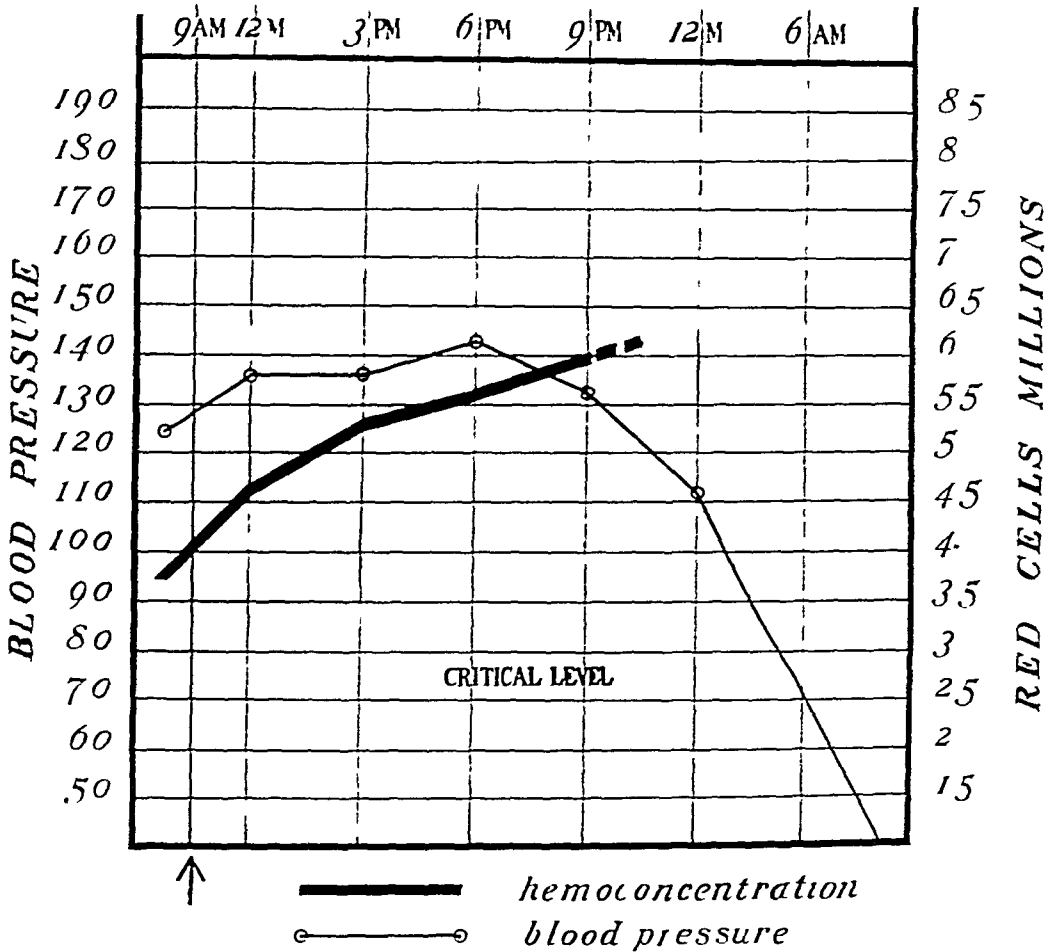


CHART 3—Showing the curves of hemoconcentration and blood pressure during the development of shock after colonic resection (arrow)

In this instance the concentration of the blood indicated impending circulatory deficiency at 12 M which was 12 hours before arterial pressure gave a similar indication. The mechanism of compensation was apparently adequate until about 9 P M by which time hemoconcentration of 60 per cent had developed. Yet at this time the blood pressure was still at a normal level.

Four grams of minced muscle substance, per kilogram of body weight, was introduced directly into the abdominal cavity of a normal dog through a short incision. Progressive concentration of the blood began almost immediately and had reached a degree of 15 per cent three hours later, at which time the blood pressure was at its highest point. The hemoconcentration had reached its maximum almost four hours before the blood pressure had declined to a critical level (70 to 80 Mm Hg). The course of the hemocon-

centration and blood pressure is shown graphically in Chart 2. Repetitions of this experiment gave uniformly similar results. In every instance the maximum concentration of the blood occurred several hours before the blood pressure sank to the critical level.

I have had opportunity to compare hemoconcentration with blood pressure readings in a number of clinical cases during the development of circulatory deficiency of the shock type. In each instance examination of the blood

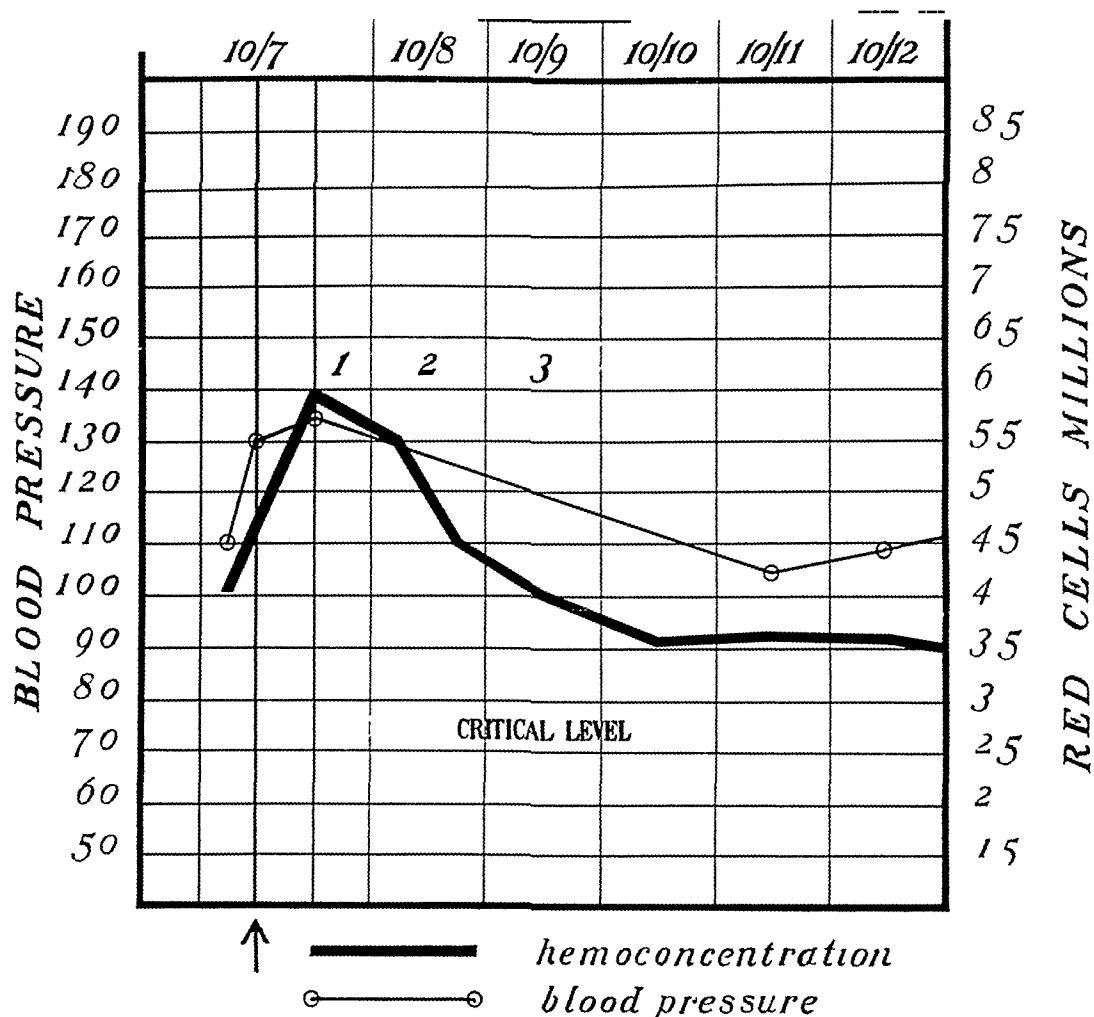


CHART 4—Showing the curves of hemoconcentration and blood pressure after operation (rectal resection for carcinoma, arrow) followed by recovery.

Note the immediate rise in concentration indicating the imminence of circulatory failure and the accompanying rise in arterial pressure indicating active compensation. Transfusions of blood and glucose in saline intravenously were administered after the operation and on the next day (1 and 2). Saline hypodermoclysis was administered on the following day (3).

forecast the development of the shock several hours to several days before the blood pressure declined notably. A few instances will be cited.

A white female, age 54, had been prepared for colonic resection by a previous colostomy operation. The resection under ether anesthesia was finished in 35 minutes. The patient's condition as indicated by pulse, respiration and blood pressure was satisfactory on return to her room. The blood pressure was not only well maintained, it actually *increased* for several hours so that at 6 00 P M it was at its highest point. Meanwhile hemoconcentra-

tion had developed steadily (Chart 3) The erythrocytic count rose from 3,820,000 before the operation to 5,500,000 nine hours later—a concentration of more than 40 per cent The concentration of the blood three hours after the operation forecast the impending circulatory collapse 12 hours before compensation failed Death occurred by shock 26 hours after the operation

In another case, a rectal resection for carcinoma, hemoconcentration of 36 per cent occurred within a few hours, while the blood pressure was at its

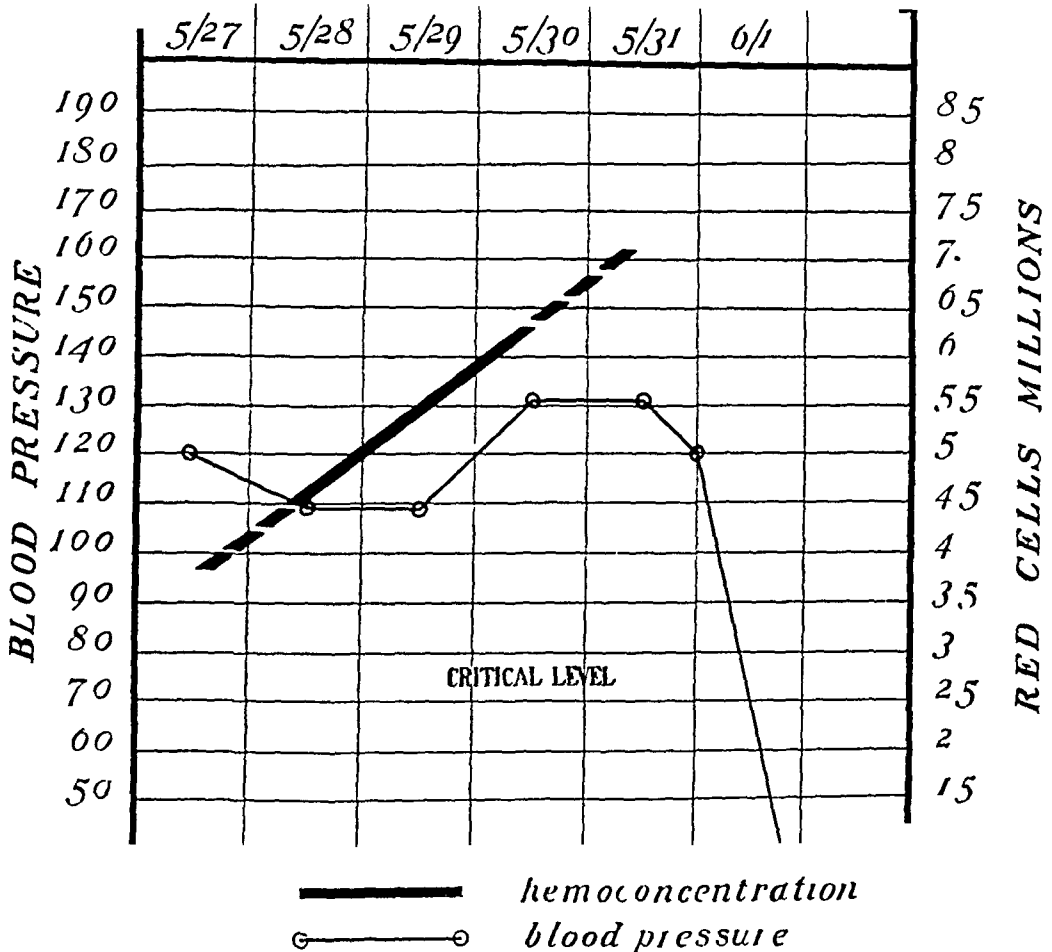


CHART 5—Showing the curves of hemoconcentration and blood pressure incident to icterus gravis. Time is shown in calendar days. Only two counts of erythrocytes were made. The heavy solid line connects them.

In this instance hemoconcentration of 40 per cent was accompanied by a compensatory rise in arterial pressure, and occurred two days before death. Note the precipitate fall in blood pressure when compensation failed.

highest recorded point (Chart 4). Transfusions of blood and repeated intravenous infusions of glucose in saline after the operation, and on subsequent days, were followed by recovery.

Circulatory failure incident to systemic intoxication was illustrated in an instance of icterus gravis, with fatal termination on the sixth day of hospitalization. The blood count on May 28, the day after admission, was 4,490,000. Two days later it had risen to 6,240,000—an increase of 40 per cent. During this time the blood pressure rose from 110 to 130 mm Hg. Two days later the blood pressure had declined only to 120 but the decline continued precipi-

tately, ending in death (Chart 5) Hemoconcentration in this instance preceded the circulatory collapse by two days, during which time the blood pressure gave no intimation of impending failure of compensation

SUMMARY—I have reviewed all records of hemoconcentration or acute erythrocytosis which could be found in medical literature, only a few of which have been cited in this paper The evidence summarized from these reports indicates that hemoconcentration is related etiologically to the mechanism by which the syndrome of shock develops in various clinical conditions Most of the authors attributed the hemoconcentration to the leakage of plasma through endothelium which had been rendered abnormally permeable by some injurious agent or condition

Our experimental studies have included intraperitoneal introduction of muscle, liver and other tissue substances, injections of watery extracts of normal tissues, of bile and its salts, peptone, bacterial cultures and toxins, histamine, snake venoms, and drugs such as emetine, veronal and other barbiturates They also included burns, trauma, intestinal manipulation and obstructions, and the effects of proteins in sensitized animals

Regularly, and without exception, the agents and conditions mentioned produced hemoconcentration This appeared early, and its degree was proportional to the apparent illness of the animal When recovery followed, the blood returned to its normal composition When death resulted, the post-mortem findings were those which we²⁸ have shown to be characteristic of shock

It appears that any agent or condition which affects capillary endothelium adversely will produce the syndrome of shock if that effect is produced systemically or in extensive visceral areas Both the experimental and clinical observations indicate that hemoconcentration is the surest and earliest clinical sign of endothelial damage of sufficient extent or degree to impair the efficiency of the circulation

It is strange that a phenomenon which is so grave in its import, so common in its occurrence, and so easily demonstrated, has not been utilized by physicians in their clinical studies of patients

CONCLUSIONS

Arterial blood pressure is not an accurate criterion of the presence of shock The latter may be present while the blood pressure is well maintained or is even at its highest recorded point

Hemoconcentration is progressive, it is an index of the degree of shock, and it subsides to normal as shock is abated Also it furnishes a means for distinguishing between shock and hemorrhage In the latter condition the blood is diluted to a degree proportional to the effects of the hemorrhage

The presence of hemoconcentration is the earliest clinical sign of shock It is easily detected, is regularly present before other signs appear and results from the same mechanism which causes shock Its use as a clinical test facilitates the early recognition and treatment of shock

REFERENCES

- ¹ Moon, Virgil H Shock and Related Capillary Phenomena New York, Oxford University Press, 1938
- Idem* Shock, Its Mechanism and Pathology (A Review) Arch Path, 24, 642, 794, 1937
- ² Baraduc, H Des causes de la mort à la suite des brûlures superficielles Union Med, 18, 321, 1863
- ³ Tappeiner Veränderungen d Blutes u d Muskeln nach angedensten Hautverbrennungen Centralbl f d med Wissensch, 19, 385, 1881
- ⁴ Wilms, M Mitt a d Grenzgeb d Med u Chir, 8, 393, 1901
- ⁵ Locke, E A Blood Examination in Ten Cases of Severe Burns Boston M and S J, 147, 480, 1902
- ⁶ Becky, K, and Schmitz, E Klinische und chemische Beiträge zur Pathologie der Verbrennung Mitt a d Grenzgeb d Med u Chir, 31, 416, 1919
- ⁷ Underhill, F P, Carrington, G L, Kapsinow, R, and Pack, G T Blood Concentration Changes in Extensive Superficial Burns Arch Int Med, 32, 31, 1923
- ⁸ Simonart, A Étude expérimentale sur la toxémie traumatique et la toxémie des grands brûles Arch Internat Pharmacodyn Therap, 37, 269, 1930
- ⁹ Moon, Virgil H Shock Syndrome in Medicine and Surgery Ann Int Med, 8, 1663, 1935
- ¹⁰ Wilson, W C, Rowley, G D, and Gray, N A Acute Toxemia of Burns Lancet, 1, 1400, 1936
- ¹¹ Harkins, Henry N Experimental Burns Arch Surg, 31, 71, 1935
- ¹² Sherrington, C S, and Copeman, S M Experimental Variations in the Specific Gravity of the Blood J Physiol, 14, 83, 1893
- ¹³ Cobbett, L Shock and Collapse Allbutts System of Med, III, 320, 1897
- ¹⁴ Vale, F P Concentration of the Blood Med Rec, 66, 325, 1904
- ¹⁵ Crile, Geo W Hemorrhage and Transfusions New York, D Appleton & Co, 1909
- ¹⁶ Henderson, Yandell Failure of Circulation Am J Physiol, 26, 260, 1910
- ¹⁷ Mann, F C The Peripheral Origin of Surgical Shock Bull Johns Hopkins Hosp, 25, 2052, 1914
- ¹⁸ Cannon, W B, Fraser, J, and Hooper, A N Some Alterations in the Distribution and Character of the Blood J A M A, 70, 526, 1918
- ¹⁹ Bayliss, W M, and Cannon, W B Note on Muscle Injury in Relation to Shock Med Res Committee, Spec Rept, Series 26, 19
- ²⁰ Bazett, M C Value of Hemorrhage and Blood Pressure Observations in Surgical Cases Ibid, 25, 181
- ²¹ Robertson, O H, and Bock, A V Memorandum on Blood Volume After Hemorrhage Ibid, 25, 215
- ²² Keith, N M Blood Volume in Wound Shock Ibid, 26, 36, 27, 3
- ²³ Bainbridge, F A, and Bullen, H B The Hemoglobin Value of the Blood in Surgical Shock Lancet, 2, 51, 1917
- ²⁴ Gray, H T, and Parsons, L Mechanism and Treatment of Shock Brit Med Jour, 1, 943, 1071, 1912
- ²⁵ Cope, Z Clinical Research in Acute Abdominal Disease London, Oxford University Press, XII, 164-206, 1927
- Idem* A Criticism of Current Views of Shock and Collapse Proc Roy Soc Med, 21, 599, 1928
- ²⁶ Freeman, N E, Shaw, J L, and Snyder, J C Peripheral Blood Flow in Surgical Shock Jour Clin Invest, 15, 651, 1935
- ²⁷ Moon, V H, and Kennedy, P J Pathology of Shock Arch Path, 14, 360, 1932
- Idem* Changes in Blood Concentration Incident to Shock J Lab and Clin Med, 19, 295, 1933
- ²⁸ Moon, V H Shock A Definition and Differentiation Arch Path, 22, 325, 1936

DERMOID CYSTS OF THE VERTEBRAL CANAL[†]

EDWIN B BOLDREY, M D, AND ARTHUR R ELVIDGE, M D

MONTREAL, CANADA

FROM THE MONTREAL NEUROLOGICAL INSTITUTE AND THE DEPARTMENT OF NEUROLOGY AND NEUROSURGERY MCGILL UNIVERSITY, AND THE MONTREAL GENERAL HOSPITAL, MONTREAL CANADA

SINCE Cruveilhier's⁶ description of an intracranial "tumeur d'apparence peilée" (1829), dermoid cysts have been encountered frequently in the brain. A spinal dermoid, however, is still a rare operative or autopsy finding. Since 1875, the presence of dermoid or epidermoid cysts in the vertebral canal has been reported in 40 instances, the present contribution of three such cases being included. This paper presents a summary of the records and a brief consideration of the anatomical and clinical aspects of these tumors.

Bostroem's² term "dermoid" and "epidermoid" (1897), currently more acceptable than Muller's²⁹ "cholesteatome" (1838), denotes a group of congenital growths which "commonly originate by the inclusion of a portion of ectoderm during closure of embryonal fissures, or at the point of union of ectoderm with other structures along the course of ectodermic invagination or from persistent embryonal ectodermal structures" or from trauma or teratomatous remnants (Ewing,¹¹ 1931). The type and location of the cyst appear related to the age of the fetus at the time of the inclusion error. They may be single or multiple, they may contain any or all of the products of the skin and its glands, though epidermoids do not as a rule contain hair.

In this presentation we have not differentiated between dermoid and epidermoid. We have assumed the accuracy of the pathological diagnosis in all instances. The following cases have been previously reported[†]

CASE REPORTS

Case 1—Eppinger,¹⁰ 1875. This case is referred to by Critchley and Ferguson.⁵ We have been unable to corroborate the reference because the article is not available.

Case 2—E. Chiari,⁴ 1883. A male, age 33, had had symptoms of a "transverse myelitis" for 19 years. A subpial cholesteroma 4 cm long, extending from the fourth to the sixth thoracic nerve segments, was discovered postmortem. It was adherent to the pia mater at the point of greatest circumference and came into close relationship with the ependyma of the central canal.

Case 3—Muscatello,³⁰ 1893. A female, age 5 months, was previously examined for a thoracic spina bifida. An incidental finding was an extradural cholesteromatous cyst the size of a large pea located over and attached to the periosteum of the fifth lumbar vertebra.

Case 4—E. Trachtenberg,⁴³ 1898. This unusual case was a male, age 55, with a history of symptoms of spinal cord compression for four years. Autopsy revealed multiple intra arachnoid and medullary dermoids and epidermoids. These were small, and extended for a considerable distance along the spinal canal and into the cranial cavity.

Case 5—W. H. White and A. D.ripp,¹⁷ 1900. A male, age 30, had been suffering for four years from Hodgkin's disease. There was a history of rapid loss of strength for a period of three months, culminating in a complete paralysis and anesthesia below a point three quarters of an inch below the nipples. There were shooting pains in the chest and upper extremity with superficial tenderness over the spinous processes of the second, third and fourth dorsal vertebrae. Surgical

Submitted for publication July 8, 1938.

* Read by title at the meeting of the American Neurological Association, Atlantic City, New Jersey, May 2-4, 1938.

† Since this article was submitted for publication two more cases have been added to the literature.

intervention revealed a tumor at the level of spinal tenderness which, when sectioned, proved to be a large dermoid cyst. It was too large for removal at one stage. Two months after the first operation a second was performed which resulted fatally.

Case 6—N S Ivanoff,¹⁰ 1903. Quoted by Lauterberg²³ (1923) and Gross¹⁵ (1934). Autopsy upon this meningoencephalic monster revealed a cavity, lined by several layers of flat epithelial cells, traversing the entire cord and medulla. The cytoplasm of the lining cells contained a horny substance and hair follicles were seen. The abnormality was described as a cholesteatoma.

Case 7—F Raymond, L Alquier and V Courtellemont,³⁵ 1904. A male, age 32, had had symptoms indicating an intracranial abnormality for two years. At autopsy there was found a large frontal lobe dermoid with small meningeal dermoid nodules in the spinal subarachnoid space. These incidental spinal findings were unrelated to the symptoms of which he complained. In this case, small cholesteatomatous masses were reported in the spinal fluid on puncture.

Case 8—F Berkil,¹ 1906. A female, age 27, had had a "transverse myelitis" type of symptom complex for eight years before investigation. A subdural cholesteatoma, 10x3 cm in size, was found (probably at autopsy) in the substance of the conus medullaris attached to the central canal and the meninges. This unusual report was summarized by Lauterberg, Salotti,³⁸ and Marinesco and Dragulesco.²⁵

Case 9—Harrichhausen,¹⁷ 1909. A female, age 23, had had pain in the left leg for nine years, followed by bilateral leg weakness and hyperaesthesia at the seventh thoracic segment. At postmortem examination an intramedullary dermoid, 5x2½ cm, cylindrical in outline and involving the central canal and the pia, was discovered at the level of the first lumbar vertebra. An interesting associated condition was redoubling of the spinal cord.

Case 10—K Frick,¹¹ 1911. A female, age 64, died after a nine year history of spastic paraplegia and anesthesia of the lower extremities. At autopsy a subdural dermoid was found pressing the cauda forward at the level of the second to fifth lumbar vertebrae.

Case 11—T von Verchely,³⁵ 1913. A male, age 15, had a double spinal cord cyst "the size of an apple" in the lumbar region. Of these cysts, one was a true dermoid while the other was a "forerunner of a neuroepithelioma." These were encased in extradural fat and were connected by a canal which bore no lining epithelium. The findings were postmortem. Marinesco and Dragulesco regard this case as an exceedingly important one because of the probability of fetal inclusions and teratoid formations. It is presented as a dermoid by its author, however, and we include it here.

Case 12—W L Robertson and S D Ingram,³⁶ 1916. A female, age 19, had had a dragging sensation in the left leg and back beginning five years before operation. When first seen, she had paralysis and anesthesia of both legs. A subdural cholesteatoma "5½x1 inches in dimension was found among the nerve roots of the lumbar region."

Case 13—C Elsberg,⁹ 1917. A female, age 60, had had occipital pain for three years. For six months there had been weakness and numbness in the right arm. Later, bladder trouble, generalized numbness and left sided weakness appeared. A subdural dermoid extending from the fourth cervical vertebra into the occiput was found at operation. The intracranial portion was removed later. (The author draws attention to the lack of respiratory symptoms.) The patient died six months afterwards.

Case 14—Guizzetti,¹⁶ 1921. This case, reported by Salotti (1927), was that of a female, age 39. No symptoms were mentioned but there was found a large dermoid, 7x2 cm, attached to the pia meninges in the lumbosacral region.

Case 15—W Lauterberg,²³ 1922. A male, age 7, was found to have an epidermoid cyst 12x10x8 mm in the region of the cauda equina, in the subdural space. It contained cholesterol crystals at its center and had a lamellated structure at its periphery. An epidermal membrane could be demonstrated over but a small part of the structure. The tumor was an incidental finding at autopsy after death due to an encephalitis.

Case 16—G Marinesco and Dragulesco,²⁵ 1924. A male, age 30, had been ill for six months with weakness of the lower extremities. He was operated upon and a subdural cholesteatoma was found at the level of the ninth dorsal vertebra. Pieces of it were removed. The patient died seven years later. At necropsy a tumor was found at the level of the tenth and eleventh dorsal vertebrae where it had destroyed the cord. Below, the cord appeared normal, above, there were syringomyelic changes.

Case 17—Drl Boz,⁷ 1926. The case is that of a dermoid cyst in a female, age 42. This incredibly huge mass extended from the seventh thoracic vertebra to the cauda equina and was 17 cm in length and 12 cm in circumference. Salotti, who reports this case, points out that the tumor had dilated the intravertebral space.

Case 18—N Melnikoff Raswedenkoff,²⁶ 1926 (reported in 1931). In a discussion of 17 cases of dermoid and epidermoid cysts of the central nervous system, mention is made of an intramedullary epidermoid. This was in a male, age 26, who had been afflicted with paraplegia. A cyst, 8x10 cm, was found between the fifth and sixth dorsal interspaces.

Case 19—A Salotti,³⁸ 1927. A male, age 31, had had regional anesthesia and decubitus ulcers for 17 years. A tumor was localized at the twelfth thoracic vertebra. At operation, a dermoid cyst 12x2½ cm in size was removed. The patient died shortly afterwards due to septicemia from his decubitus ulcers.

Case 20—T A Shallow,⁴⁰ 1928. This is a case of a small dermoid cyst in a male patient age 30. Symptoms were of one year's duration and were those of spinal cord compression associated

with lumbar pain. At operation, a cyst was found surrounded by roots of the cauda equina. It was removed successfully. There was great relief from pain in the back and the patient was walking in 1 month. The impaired bladder function was improved after the first year.

Case 21—M. Critchley and E. R. Ferguson,⁵ 1928. A male, age 15, with a history of "meningitis" at age 3, and an unexplained paralysis of the legs at age 7, developed influenza. After three weeks in bed he developed severe leg pains and could not stand or walk unassisted. Although there was no sphincter loss, signs of pyramidal irritation were found in the lower extremities and there was a sensory level at the eighth thoracic segment. A noncapsulated tumor, later diagnosed "true epidermoid," lay beneath the laminae of the seventh and eighth thoracic vertebrae. It was subdural and bound up with the pia arachnoid. Recovery was complete.

Case 22—L. Delrez,⁸ 1929. The patient was a female, age 5. For two months prior to investigation, she had had sensory and motor symptoms of spinal compression. She was operated upon and a dermoid cyst found extending from the level of the third lumbar vertebra to the sacrum. The patient recovered from the operation but unfortunately there was an associated sarcoma of the kidney.

Case 23—John Fraser,¹² 1930. A male, age 22, had had midback discomfort for one year. This had become girdlelike in the region of the groin, with shooting pains and a numb feeling aggravated by activity. General clonic contractions of both legs on going to sleep, a disturbance of gait and loss of sphincter control appeared shortly before investigation. At operation an epidermoid cyst, 9.5 x 0.7 cm in maximum diameter, was discovered in the posterior median fissure at the level of the eleventh thoracic nerve segment.

Case 24—P. Pitotti,³³ 1930. At the autopsy on a male, age 26, who had died of pyelonephritis, a large sacral dermoid cyst was found, compressing the cauda equina. There is no history of related symptoms.

Case 25—P. L. Hipsley,¹⁸ 1932. A female, age 3, had had a discharging sinus in the upper back, and pain in the left chest for several weeks. Four weeks before examination, difficulty in walking appeared. Lumbar puncture yielded xanthochromic fluid which coagulated on standing and contained 72 cells per cu. mm., 80 per cent lymphocytes and 20 per cent neutrophilic granulocytes. Lipiodol injected into the cisterna magna was arrested at the level of the seventh cervical vertebra. At operation a dermoid cyst, 18 x 12.5 mm in size, was removed. It was firmly adherent to the dura. The postoperative course was uneventful.

Case 26—J. Michelsen,²⁷ 1932. Following spinal anesthesia, this female, age 32, developed a motor and sensory incapacity. After a three and one-half year remission the symptoms recurred. At operation a mass, later identified as a "cholesteatoma," was found arising from the pia in the midline, posteriorly, at the eleventh and twelfth thoracic vertebrae. Death followed removal.

Case 27—A. H. Schroeder,³⁹ 1932. A female, age 35, had had weakness which commenced in the right leg one and one-half years earlier. The clinical findings were slight involuntary movements in the left leg and right hallux, diminished sensation below the second lumbar segment, and tender spinous processes on the eleventh and twelfth thoracic vertebrae. A "cholesteatoma" lay at the end of the cord beneath the laminae of the tenth and eleventh thoracic vertebrae. It was successfully removed.

Case 28—W. J. Mixer,²⁸ 1932. A male, age 23, had a dull, low back pain commencing six years previously. Later, stabbing pain and weakness were experienced in the right knee. Before operation, disability included weakness, pain and numbness in both legs and hands. There was roentgenologic evidence of bony canal dilatation. A dermoid, "the size and shape of a walnut," was found splitting the dorsum of the cord. It was evacuated and partly excised. Symptoms recurred one and one-half years later.

Case 29—P. Ottonello,³² 1933. A female, age 20, had suffered for two weeks prior to admission, with motor and sensory symptoms, including marked hyperreflexia, bilateral Babinski reflexes and vesicorectal incontinence. At operation an extramedullary dermoid 6.5 x 2 cm in size, was removed. The patient recovered. An interesting associated condition present in this case was rachischisis.

Case 30—S. W. Gross,¹⁵ 1934. For several years this male, age 44, had had pain, atrophy and weakness in all extremities. A sensory and vasomotor level, more right than left, was found at the fifth thoracic dermatome. An intramedullary dermoid projected 4 to 5 mm into the left side of the cord at the level of the disk between the second and third vertebrae. It was firmly attached at the bottom. It recurred three years later.

Case 31—H. C. Naffziger and O. W. Jones, Jr.,³¹ 1935. A female, age 60, since age 18, had complained of a weak back. At age 30, she had had "acute lumbago" followed by constant backache. At age 57, an operation for spinal bifida occulta partially relieved the weakness, numbness and muscle spasm in the right leg. One year later, the pain in the left leg became so severe that coupled with recrudescence of the remaining right-sided symptoms it prevented walking. A fusiform dermoid cyst of the cauda equina, 2.3 x 8 cm, was found to extend from the twelfth thoracic to the second sacral vertebrae. Though it could not be removed *in toto*, 45 Gm. of cheesy, hair-containing material was excised. Recovery was complete save for right-sided foot drop.

Case 32—H. C. Naffziger and O. W. Jones, Jr., 1935. For two years this female, age 27, had had increasing pain radiating from the third lumbar vertebra first to the left and then to the right leg. For 20 months she had had urinary frequency. For two months, she had been incontinent.

Röntgenograms showed a widened vertebral canal in the region of the twelfth thoracic and first lumbar vertebrae. At operation an intradural "cholesteatoma" of the filum terminale was found extending distally from the twelfth thoracic vertebra. It contained 9 Gm of cheesy material. Calcium deposits and nerve fibers were present within its capsule. Recovery ensued except for persistent sensory changes.

Case 33—H C Naffziger and O W Jones, Jr, 1935. A female, age 33, had increasing knee, hip and sacroiliac pain accompanied by weakness and spasm of the leg muscles for nine months following chiropractic manipulations. There were no objective sensory signs. Leg and trunk movements were limited. A spinal subarachnoid block was demonstrated at the level of the third and fourth lumbar vertebrae. An intradural cholesteatoma 1.5 cm in diameter was removed from among the roots of the cauda equina. Recovery was complete.

Case 34—H C Naffziger and O W Jones, Jr, 1935. A male, age 45, had had 'bladder symptoms' for 16 years. In the decade preceding investigation there had developed perineal numbness, followed by paroxysmal pain, weakness and anesthesia in the legs. On admission, skin sensations were absent in the first four sacral dermatomes, and there were coarse fibrillations of the calf and thigh muscles. There was a spinal subarachnoid block at the first lumbar interspace. Operation revealed a dermoid cyst, 5.5 cm long filling the dural sac and attached to the conus and filum terminale. Convalescence was satisfactory.

Case 35—P Puech, A Pichet, F Visalli, and M Brun³⁴, 1936. A male, age 37, had had difficulty in walking for one year. There were sensory changes in the legs for a shorter period. Finally vesicorectal incontinence and genital changes were noted. An intramedullary dermoid at the sixth and seventh thoracic segments was curetted. 4 Gm of material being removed. The capsule was thin or absent throughout. The postoperative course was satisfactory.

Case 36—J G Love and J W Kernohan,²⁴ 1936. A male, age 40, complained of leg weakness and incontinence for an unstated period of time. A dermoid cyst was found "in the conus medullaris and filum terminale." It was excised. Convalescence was uneventful, but the neurological condition was essentially unchanged.

Case 37—R A Varshaver¹⁴, 1937. The description of this intradural cholesteatoma is not available.

We have omitted two cases cited by Steinke⁴¹ (1918) because information supplied does not allow us to determine that these cases have not been already included in our reports.

The appended cases have been studied by us.

Case 38—No 16270, R V H. Male, age 17, was admitted complaining of having had bilateral "sciatica" for several years, lumbar pain for 15 months, complete right leg paralysis and paresis of the left leg for three to four months, recent fecal incontinence and urinary retention.

Physical Examination demonstrated absent knee jerks, atrophy and absent faradic response in the right peronei, contractures in the right foot, priapism, and anesthesia over the legs, backs of thighs, buttocks and perianal regions.

Operation—An intradural tumor, lying between the second and fourth lumbar vertebrae, was only partly removable. It was described by Professor Adams as an "epithelial inclusion cyst of the spinal canal within the dura mater." Microscopic examination leaves no doubt, however, but that it was an epidermoid cyst.

The postoperative course was satisfactory but the symptoms were not alleviated. This case, found in 1908, Dr C K Russel kindly allows us to present.

Case 39—No 5374-33, M G H. Male, age 45, was admitted to the "M" service of the Montreal General Hospital complaining of fecal incontinence, urinary frequency for six years, and ulceration of the buttocks for two weeks. The onset of symptoms immediately followed removal of an "anal fistula" and left herniotomy and orchidectomy. Perineal and leg numbness were noted while still convalescing, genital anesthesia was first observed three weeks afterwards. A few weeks later difficulty in complete bowel and bladder evacuation appeared. There was likewise disturbance of sexual function.

Four years before the present admission, there was twitching of the leg muscles on fatigue. More recently this had been intermittent regardless of activity. During the last 18 months, he had had leg weakness, urinary frequency, dribbling, and fecal incontinence after cathartics. The immediate cause for seeking relief was the appearance of the rapidly spreading ulcers on the buttocks.

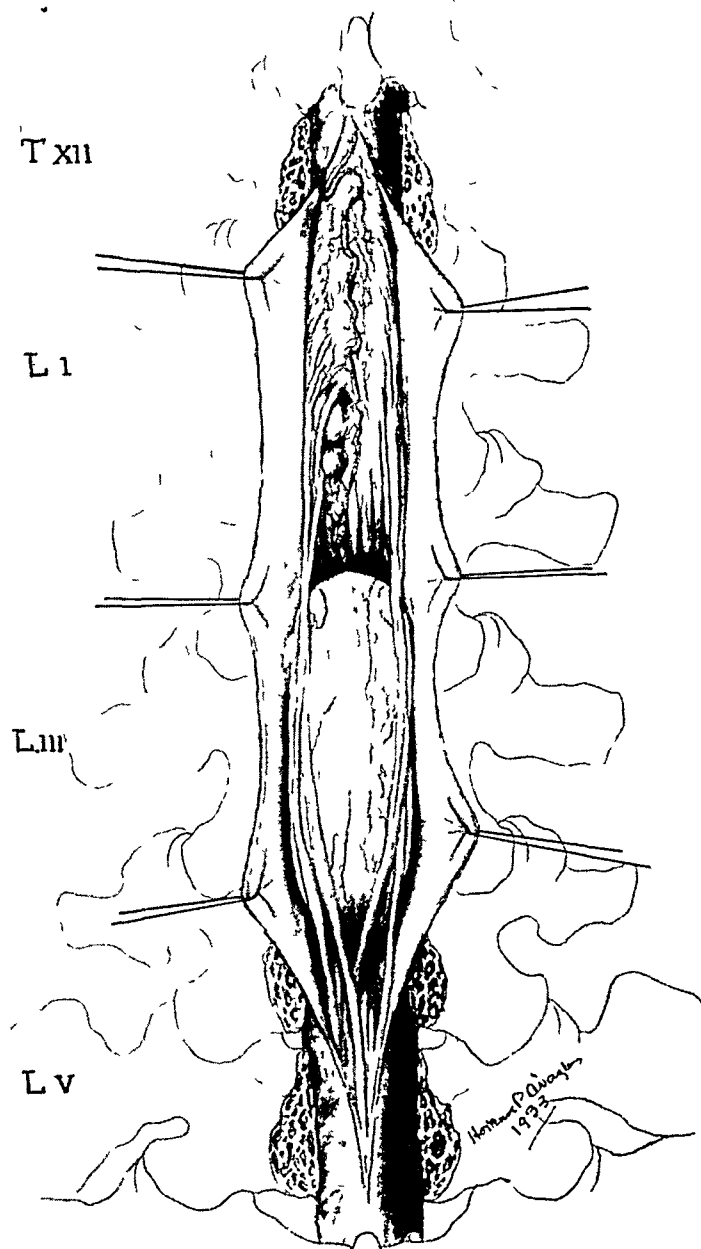


FIG 1—Case 39 Dermoid cyst of the cauda equina in situ
The cyst and conus medullaris are represented about one segment
too high in this drawing



FIG 2—Case 39 Section through the wall of the cyst showing desquamated material
in the lumen

Physical Examination demonstrated pressure sores on each buttock, a greatly distended bladder, complete cutaneous anesthesia in the third, fourth and fifth sacral segments, partial cutaneous anesthesia in the first and second sacral segments, atrophy and fibrillary twitchings of leg muscles, and slight increase of "tone" in the left leg. Deep reflexes in the legs were hyperactive. The cremasteric reflex was present. Lumbar punctures were performed with the results as charted (Table I).

TABLE I
RESULTS OF LUMBAR PUNCTURES

Lumbar Interspace	September 15	September 22	September 27	September 28
1	Normal	Not tested	Complete block	Complete block
2	Dry tap	Partial block	One drop of creamy material*	Partial block
3	Normal	Complete block	Complete block	Complete block
4	Normal	Not tested	Not tested	Not tested
5	Normal	Not tested	Not tested	Not tested

* Smears made of the turbid substance obtained September 27 showed an occasional cell shadow in an amorphous material.

Operation—Laminectomy was performed. Beneath the third and fourth lumbar laminae was an oval-shaped, yellowish mass, 5×3 cm in size, anchored among the posterior roots of the cauda equina by thin membranous attachments (Fig. 1).

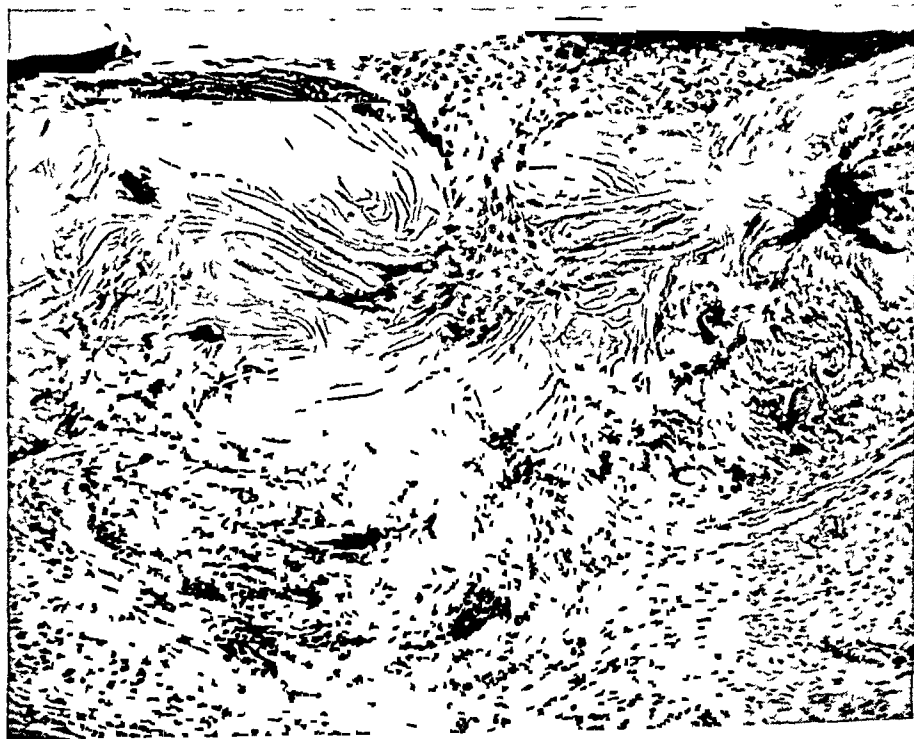


FIG. 3—Case 39. Section showing epidermis and hyalinized connective tissue beneath.

Operative Pathology—The tumor consisted of a soft, cheesy material in a thin, translucent capsule, on the outside of which clung flakes of a similar substance. Between this cyst and the conus medullaris was a greenish cord, irregularly cystic, forming a bulbous swelling against the side and tip of the conus. It adhered to the upper two-thirds of the tumor. The tumor and cystic cord were completely removed.



FIG 4—Case 39 Section through cyst wall showing a hair follicle in hyalinized subepidermal connective tissue



FIG 5—Case 39 Section through ventriculus terminalis

The postoperative course was uneventful. A year later there was still vesicorectal incontinence, weakness and anesthesia corresponding with the complete level on admission.

Pathologic Examination—Microscopic The main tumor is a typical dermoid cyst, with walls of stratified squamous epithelium and containing hair, sebaceous material, and sheets of desquamated stratified keratin (Fig 2). The epidermis lies upon a thin bed of fibrous connective tissue which is hyalinized in some regions (Fig 3). One hair follicle has been seen in cross-section (Fig 4).

The cystic cord is chiefly composed of loose glial tissue, the cells resembling small astrocytes. An occasional large astrocyte and nerve cell is to be seen. Corpora amylacea are present. A large empty cyst, representing the ventriculus terminalis (Kernohan,²² 1924), is eccentrically placed in this tissue. It is lined by layers of poorly preserved ependymal cells on a connective tissue substratum. Immediately beneath the ependyma, macrophages containing yellow pigment lie in an interrupted sheet.

Sections taken further caudad show a general structure of medullary tissue and a narrowed cystic cavity representing central canal or ventriculus terminalis (Fig 5). Corpora amylacea are surrounded by pigmented macrophages. Glial tissue wraps about the ependymal cavity to form the general shape and structure of the spinal medulla.

Case 40—No 2304, M N I The parents of this male child, age 2½, noticed a pigmented, elevated spot over the lumbosacral spine shortly after birth. Nine months before admission a discharge appeared at this point and continued intermittently until admission. For five months before admission, attacks of chills, fever, opisthotonos and vomiting occurred at two to three week intervals. The appearance was of recurring meningeal irritation. When admitted he had already had a right-sided hernial repair.

When first seen he lay with his legs drawn up and resented any attempt to extend them. He had neck stiffness and bilateral absence of ankle jerks. Pus could be expressed from the draining sinus in the lumbosacral region.

Operation—A dermoid cyst was found filling approximately two-thirds of the vertebral canal. It lay between the conus, at the twelfth thoracic vertebra level and the second sacral spine. Though subdural, it connected with the skin surface, through a spina bifida of the fifth lumbar vertebra, by means of the sinus tract. It was opened and was found to contain cheesy material, hair and pus, in which were numerous gram-positive cocci. Patches of purulent exudate were found all along the subarachnoid space as high as the ninth thoracic vertebra. Lower down, pus was also found epidurally and subdurally.

The right side of the conus continued, for several centimeters, as a greenish core of homogeneous tissue—apparently an extension of the spinal cord.

Many of the roots forming the cauda equina were so intimately adherent to the wall of the cyst that only a subtotal removal was possible. Due to the infection, a stormy convalescence followed, but he was discharged in a plaster corset four and one-half months later.

Pathologic Examination—The removed tissue was seen to consist of stratified squamous epithelium, flakes of keratin, amorphous debris, and gram-positive cocci among numerous polymorphonuclear leukocytes. *Diagnosis* Dermoid cyst, infected.

Discussion of Cases Presented—Though the actual removal was successful, each of our patients has persisting sequelae. In each instance, the dermoid lay among the roots of the cauda equina. Two of our patients had had an inguinal hernia operated upon before the dermoid was discovered. Twice the cyst was attached to the end of the cord.

In our second case, we were unable to identify any continuation of the filum caudal to the dermoid. Cephalad, the filum was cystic and separable from the conus by a line of cleavage. The ependymal cysts and transition from fibroblastic into glial tissue in this case are important pathologically.

Clinical interest centers about the fortuitous needle biopsy and inconstant subarachnoid block. As to pathogenesis, we feel that the "anal fistula" must be assumed to have been a pilonidal cyst and part of the original cord of epithelium from which the dermoid was separated. Radical excision of this pilonidal cyst released intravertebral attachments. Thereafter, the growing dermoid suspended from the cord possibly tugged on the conus and produced the symptoms by repeated cord injury. The tumor, therefore, represents the original point of attachment of the filum to the skin, from which it was separated in the normal growth processes. This theorization has adequate support in the work and writings of embryologists as Streeter⁴² (1919), Keith²¹ (1933), Jordan and Kindred²⁰ (1926) and Fiazei¹³ (1931).

The cystic connection between cord and dermoid seems analogous to the vestige particularly described by Fiazei, who states that part of the coccygeal cord is carried up on the conus to form a small addendum containing the distorted remains of the central canal. Bearing this observation in mind, the gradual transition from glial tissue into the connective tissue of the cyst wall assumes unique significance.

The features of the third case are the associated infected sinus and the spina bifida. The fact that this dermoid extended to the skin as an ectodermal sinus relates it to the dermal sinuses as described by Walker and Bucy⁴⁶ (1934). We agree that these sinuses and the dermoids are but stages in the same developmental anomaly.

Discussion—Of these 40 patients, 21 were male, 16 were female and in three the sex was not mentioned. The age at discovery, by decades, was first decade, six cases, second decade, four cases, third decade, eight cases, fourth decade, 11 cases, fifth decade, five cases, sixth and seventh decades, four cases, unknown, two cases. The age at onset of symptoms was first decade, eight cases, second decade, eight cases, third decade, ten cases, fourth decade, seven cases, fifth and sixth decades, five cases, unknown, two cases. The extreme ages at discovery range from birth (an anencephalic monster) to 62 years. The period of symptoms varies from two weeks to 19 years. A long history is more common. Five patients had no symptoms or signs referable to the tumor.

The tumor size ranged from 17x12 cm. to tiny subpial growths of from 4 to 5 mm. in diameter. Two patients had multiple cysts. Of the tumors where meningeal position is mentioned, two were extradural, 13 were subdural, 13 were subarachnoid and nine were subpial. Twenty-nine of the solitary cysts were below the level of the sixth thoracic vertebral body. All or part of 20, were in the lumbosacral region. Of the 24 patients operated upon, 19 recovered. Three of these had a recurrence, discovered in one and one-half, three, and six years, respectively. In eight instances, including the three with recurrence, the cyst could not be completely removed because of its peripheral attachments.

Associated conditions have included anencephaly, Hodgkin's disease, encephalitis, influenza, intracranial dermoids, neuro-epithelioma, spina bifida,

pilonidal cyst, infected sinus tract, dilatation of the vertebral canal (three cases), inguinal hernia, and sarcoma of the kidney. All but the last were connected in some way with the tumor and its diagnosis. From this information we conclude that apparently some anomaly of growth may occur which leaves ectodermal cell rests in such a position that the cyst resulting from their proliferation may lie anywhere between the central canal of the spinal cord and the skin surface. Symptoms usually appear before the fortieth year, and most frequently point to a slowly expanding lesion in the lumbosacral segments of the vertebral canal. Sharp, shooting pains in the leg, often circumscribed in extent, are a frequent cause of complaint. Important associated findings in such patients are spina bifida, lumbosacral dimple, and inguinal hernia. The diagnostic importance of a midline lumbosacral or pilonidal sinus is to be emphasized. When such cysts are found at operation their potential multiplicity and tendency to recur if incompletely removed, must be borne in mind.

SUMMARY

(1) A review and discussion of the literature, including 37 cases of dermoid cyst of the vertebral canal, is made. Three cases are added.

(2) These cysts produce symptoms of slowly progressive spinal cord compression beginning usually in the second, third or fourth decade of life. They may be present at birth or may not give trouble till the sixth decade.

(3) Spinal dermoids have a wide range of size. They may be multiple. They may appear anywhere between the central canal of the spinal cord and the skin surface, and usually are in the lumbosacral region. They may dilate the bony canal. They may be related to dermal sinuses and pilonidal cysts of the coccygeal region. Inguinal hernia may be associated with cysts in the cauda equina.

(4) Removal must often be incomplete. Therefore, recurrence is not infrequent.

BIBLIOGRAPHY

- ¹ Berkal, F. Cholesteatoma de cauda equina. *Casopis lekaru ceskych*, Nr 11, 1906 (Unavailable, mentioned by Lauterberg and Salotti.)
- ² Bostroem, E. Über die Pialen epidermoide, dermoide, und lipome und duralen dermoide. *Centrabl f allg Path Anat*, 8, 1, 1897.
- ³ Brock, S., and Klenke, D. A. A Case of a Dermoid Overlying the Cerebellar Vermis. *Bull Neurol Inst New York*, 1, 328, 1931.
- ⁴ Chiari, E. Centrales Cholesteatoma des entwickeltes auf und absteigender Degeneration. *Prager Med Wchnschr*, 39, 378, 1883.
- ⁵ Critchley, M., and Ferguson, F. R. The Cerebrospinal Epidermoids (Cholesteatomata). *Brain*, 51, 334, 1928.
- ⁶ Cruveilhier, Jean. *Anatomie Pathologique du Corps Humain*. 1, Livraison II, Planche 6, J. B. Bailliere, Paris, 1829-1835.
- ⁷ Dal Bo. Cisti dermoide colesteatomatosa del Midollo spinale. *Comunicaz al VII Congr della Soc Ital di Neurologia*, 1926 (Not available, quoted by Salotti.)
- ⁸ Delrez, L. Kyste dermoide rachidien et sarcome du rein chez le même enfant. *Liege Med*, 22, 1667, 1929.

- ⁹ Elsberg, C A Tumors of the Spinal Cord Hoeber, New York, 1925
- ¹⁰ Eppinger Prag Vierteljahrschrift, 1875
- ¹¹ Ewing, James Neoplastic Diseases W B Saunders, Philadelphia, 1931
- ¹² Fraser, John A Cystic Dermoid Tumor of the Spinal Cord Surg, Gynec and Obstet, 51, 162, 1930
- ¹³ Frazer, J E A A Manual of Embryology Balliere, Tindall & Co, London, 1931
- ¹⁴ Frick K Über ein Teratom des Rückenmarks Frankfurter Zeitschr f Path, 7, 127, 1911
- ¹⁵ Gross, S W Intraspinal Dermoids and Epidermoids, with Report of a Case J Nerv and Ment Dis, 80, 274, 1934
- ¹⁶ Guzzetti, P Trattato di Anatomia Patologica di P Foa, 1924
- ¹⁷ Harriehausen Über Dermoid im Wirbelkanal neben Verdoppelung des Rückenmarks Deutsche Ztschr f Nerven, 36, 269, 1909
- ¹⁸ Hipsley P L Dermoid Cyst of Spinal Cord Australian and New Zealand J Surg, 2, 421, 1932-1933
- ¹⁹ Ivanoff, N S A Case of Cholesteatoma of the Spinal Cord J Neuropat i Psikhiatri Korsakova Mosk, 80, 1903 (Not available, reported by Lautenberg)
- ²⁰ Jordan, H E and Kindred, J E A Textbook of Embryology D Appleton Co, New York, 1926
- ²¹ Keith, Sir Arthur Human Embryology and Morphology Edward Arnold & Co, London, 5th Ed, 1933
- ²² Kernohan J W The Ventriculus Terminalis Its Growth and Development J Comp Neurol, 38, 107, 1924
- ²³ Lautenberg, W Ein Epidermoid frei im Wirbelkanal und seine Kombination mit Hirnlasionen Virchows Arch f path Anat, 240, 328, 1922
- ²⁴ Love, J G, and Kernohan, J W Dermoid and Epidermoid Tumors (Cholesteatomas) of Central Nervous System J A M A, 107, 1876, 1936 (reprint)
- ²⁵ Marinesco, G, et Draganesco (de Bucarest) Kysti epidermoide cholesteatomateux de la moelle epiniere co-existant avec un processus syringomielique Revue Neurol 43, 338, 1924
- ²⁶ Melnikoff-Raswedenkoff, N Über epidermoide und dermoide Cholesteatoma des Grosshirns und Rückenmarks mit besonderer Berücksichtigung der in der Ukraine beobachteten Fälle Virchows Arch f path Anat, 279, 702, 1931
- ²⁷ Michelsen, J Cholesteatom des Rückenmarks Deutsche Ztschr f Nerven 127, 123, 1932
- ²⁸ Mixer, W J Spinal Column and Spinal Cord Lewis Practice of Surgery, XII, Chap III, 68, 1932
- ²⁹ Muller, Johannes Über den feinen Bau und die Formen der krankhaften Geschwulste Berlin, 50, 1838
- ³⁰ Muscatello, G Über die angeborenen Spalten des Schädels und der Wirbelsäule Arch f klin Chir, 47, 259, 1893
- ³¹ Naffziger, H C, and Jones, O W, Jr Dermoid Tumors of the Spinal Cord Arch Neurol and Psychiat, 33, 941, 1935
- ³² Ottonello, P Contributo alla conoscenza della sindrome rare da tumori endriogenetici, dermoide spinale associato a rachischisi, decorso atipico, efficace intervento chirurgico Riv di pat nerv, 41, 512, 1933
- ³³ Pitotti, P Su di caso di colesteatoma del midollo spinale Rivista di Patologia Nerve e Ment, 35, 36, 1930
- ³⁴ Puech, P, Pichet, A, Visalli, F, et Brun, M Cholesteatome intramedullaire Intervention Guérison Rev Neurol, 66, 56, 1936
- ³⁵ Raymond, F, Alquier, L, et Courtellemont, V Un cas de kyste dermoide des centres nerveux Rev Neurol, 12, 635, 1904
- ³⁶ Robertson, W E, and Ingham, S D A Case of Cholesteatoma of the Spinal Cord Pennsylvania Med Jour, 9, 408, 1916

- ³⁷ Roussy, Gustave Les cholesteatomes Bull Assoc franc pour l'etude du cancer, 5, 192, No 8, 1912
- ³⁸ Salotti, A Dermoide del midollo spinale Arch ital di chir, 19, 135, 1927
- ³⁹ Schroeder, A H Colesteatoma medular Anales de la Facultad de Medecina (Montevideo), 17, 591, 1932
- ⁴⁰ Shallow, T A Dermoid Cyst of Cauda Equina with Spinal Cord Compression Surg Clin North Amer, 8, 885, 1928
- ⁴¹ Steinke, C R Analysis of 330 Collected Cases of Spinal Tumors J Nerv and Ment Dis, 47, 418, 1918
- ⁴² Streeter, G L The Formation of the Filum Terminale Am J Anat, 25, 1, 1919
- ⁴³ Trachtenberg, E Ein Beitrag zur Lehre von dem arachnoidealen Epidermoiden und Dermoiden des Hirns und Rückenmarks Virchows Arch f path Anat, 274, 1898
- ⁴⁴ Varshaver, R A Intradural Cholesteatoma Novy Khir Arkhiv, 37, 629, 1937
- ⁴⁵ von Verebely, T Ein Fall von intervertebralen Dermoidzyste Virchows Arch f path Anat, 213, 41, 1913
- ⁴⁶ Walker, A E, and Bucy, P C Congenital Dermal Sinuses A Source of Spinal Meningeal Infection and Subdural Abscesses Brain, 57, 401, 1934
- ⁴⁷ White, W H, and Fripp, A D Case of Dermoid Tumor Clinical Society's Transactions, London, 33, 140, 1900

SPINAL EXTRADURAL CYST ASSOCIATED WITH KYPHOSIS DORSALIS JUVENILIS

JAMES F. ROBERTSON, M.D., AND CHARLES P. GRAHAM, M.D.

WILMINGTON, N. C.

SPINAL extradural cysts are sufficiently rare and the results of their operative removal are so gratifying that further discussion of this interesting lesion seems warranted. Elsberg, Dyke, and Brewer¹ were the first to describe this lesion, reporting four cases, in 1934. Their search of the literature failed to reveal a single instance of a similar case on record, although Lehman,² one year later, added two additional cases and was able to find reports of three other instances of extradural cysts, only two of which probably fall into the group under discussion. Cloward and Bucy³ were the first to recognize and point out the relationship of extradural cyst as an etiologic factor in the production of bony changes within the spine characteristic of and identical with those occurring in kyphosis dorsalis juvenilis (the rounded humpback of adolescence). In their article which appeared in 1937, they cited nine other proved cases of spinal extradural cyst in addition to the one they reported, and found one other unproved and unrecognized case, originally reported by Blum. Since the publication of their paper an additional case has been reported by Kelly.⁴

In the present communication we wish to report a case of spinal extradural cyst associated with changes within the spine identical with those described by Cloward and Bucy.³

Case Report—H. H., colored, male, age 14, was referred from the Orthopedic Clinic of the James Walker Memorial Hospital, Wilmington, N. C., by Dr. Alonzo Myers of Charlotte, N. C. He was admitted to the James Walker Memorial Hospital, December 18, 1937.

Six months prior to admission the child first noticed weakness and stiffness of the right leg which gradually spread to involve the left leg and within two months had progressed into a complete spastic paraplegia. No history of trauma could be elicited. At no time had there been any pain, and the child was aware of no subjective change of sensation, although at the first examination a superficially infected, second degree burn was found over the left hip, which caused no pain at the time of its occurrence three weeks prior to admission. There had been no disturbance in the control of either the vesical or rectal sphincters. The general health of the child had been good and there was no history of recent illnesses or infections. He had received no medical attention prior to admission to the local hospital.

Examination—The child was an illiterate but cheerful, well-nourished and well-developed Negro boy. The temperature, pulse, respiration, and blood pressure were all within normal limits. General physical examination showed the head, neck, lungs, heart, and abdominal viscera to be normal. The spine was in good alignment and no evidence of a rounded dorsal kyphosis could be demonstrated.

Neurologic examination revealed the cranial nerves to be intact. The musculature and strength of the upper extremities were normal and their deep tendon reflexes were

Submitted for publication September 29, 1938

present and bilaterally equal. Hypesthesia was present below the level of the anterior iliac spines, the perception of light touch and pin-prick being diminished below this level. There was no "saddle area" of anesthesia. Kinesthetic proprioception and position-sense were completely absent in the lower extremities. There was motor paralysis of both lower extremities with marked spasticity. No muscle atrophy was discernible, but early contracture deformity was beginning to become evident. A mass reflex response could be elicited on painful stimulation. The deep tendon reflexes were markedly exaggerated and there was well-sustained clonus both at the ankle and patella. A positive Babinski sign was present bilaterally.

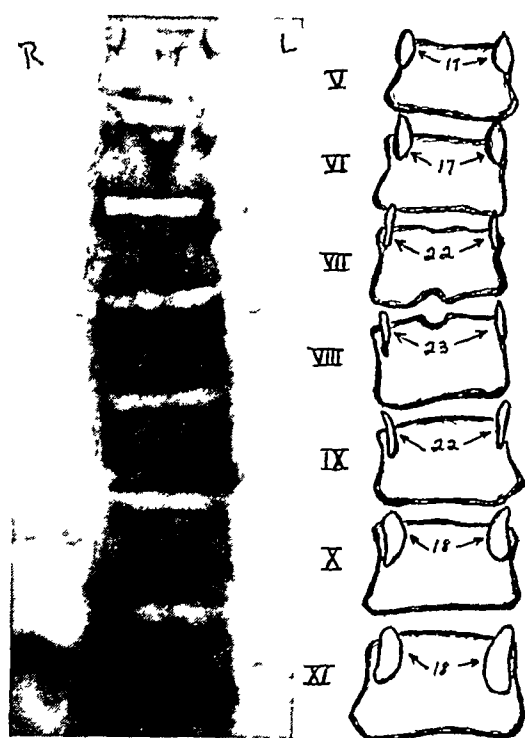


FIG 1a—Anteroposterior view of the dorsal spine. Note the thinning of the pedicles of the seventh, eighth and ninth vertebrae with a corresponding dilatation of the spinal canal. The disk between the seventh and eighth vertebrae has ruptured into their bodies.

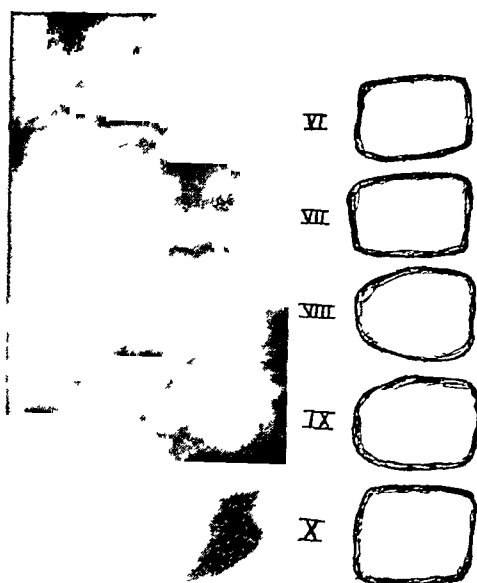


FIG 1b—Lateral view of the dorsal spine. The reproduction is not as clear as the original film but a rounding off of the anterior superior and anterior inferior borders of the eighth and ninth vertebral bodies can be seen.

Spinal puncture between the third and fourth lumbar vertebrae revealed clear, colorless fluid under an initial pressure of 70 Mm of water. There was no manometric rise on jugular compression, but a sharp response was elicited on firm abdominal pressure. The spinal fluid contained 15 lymphocytes and assayed a total protein content of 200 Mg per 100 cc of fluid.

Roentgenograms of the spine showed a slight, right lateral scoliosis in the mid-dorsal region (Fig 1a). The laminae of the seventh, eighth, and ninth dorsal vertebrae were thin and their corresponding pedicles were markedly eroded and flattened on their medial surfaces. The spinal canal was somewhat dilated between the levels of the seventh and ninth dorsal vertebrae, inclusive. The transverse diameter, as measured by the interpedicular space, reached a maximum of 23 Mm, whereas the space immediately above and below this dilatation measured only 17 Mm and 18 Mm, respectively. The intervertebral space between the seventh and eighth dorsal vertebrae was somewhat narrowed and there was evidence of rupture of this disk into the contiguous vertebral bodies. In the lateral view (Fig 1b) the contour of the spine was normal. The anterior superior

and anterior inferior borders of the bodies of the eighth and ninth dorsal vertebrae were rounded and indistinct, but definite wedging of the bodies could not be demonstrated

Diagnosis—It was plainly evident that we were dealing with cord compression, most likely due to an expanding neoplasm in the mid thoracic region

Operation—December 21, 1937 Under avertin and ether anesthesia, the laminae of D IX, D X, and D XI were exposed and removed. This brought into view a thin-walled cyst which bulged down from under the eighth neural arch, filling the spinal canal entirely from side to side. The cyst was easily pulled down from under the arch and was found to be attached to the dura by a single narrow pedicle arising from the dorsal surface of the dura near the exit of one of the posterior roots. The pedicle was cut between silk ligatures and the cyst removed. This left a greatly dilated spinal canal and the laminae over this area were seen to be very thin. The cyst was roughly the shape



FIG. 2—The patient three and one-half months after operation. Note the ability to stand on one leg unsupported, and the erectness of the spine

of an egg and measured approximately 3x4 cm. Its wall was thin and translucent and contained clear, colorless fluid. Microscopically, the cyst wall was composed of thin avascular fibrous tissue lined with a single layer of flattened epithelium similar to that of the arachnoid membrane.

Postoperative Course—Convalescence was smooth, and on the third postoperative day function began to appear in both legs, and thereafter strength and motion rapidly returned. A body encasement was applied with the spine in hyperextension and the patient was discharged, January 12, 1938, 22 days after operation. At this time the child was able to stand and walk with assistance.

Subsequent Examinations—April 5, 1938 "The child walks with a normal gait. Muscle tone normal. Position-sense good. Sensation normal. Tendon reflexes hyperactive, and there is still unsustained ankle clonus. The plantar response is down."

June 25, 1938 "Normal muscular strength. Romberg negative. Knee jerks normal. No clonus. Abdominal and cremasteric reflexes active. Carriage is erect and the spine is of normal contour."

Discussion—The clinical picture of spinal extradural cyst is remarkably constant and this feature has been emphasized in every article that has appeared on the subject. The lesion usually appears in adolescent boys between the ages of 12 and 16, but it is not unknown in girls. The cysts seem to have a predilection for the dorsal region, the majority arising from the dura in the midthoracic area usually between the sixth and ninth dorsal vertebrae. Just why they should arise in this region is not entirely clear, and we have no plausible explanation to offer. Elsberg, Dyke, and Brewer¹ advance the hypothesis that the cysts may arise either as a congenital diverticulum from the dura mater or as a herniation of the arachnoid through a defect in the dura. Cloward and Bucy³ conclude from their microscopic examination of the cyst wall that there is more evidence to support the diverticular origin, although Kelly⁵ favors the herniation theory. Direct communication between the cyst and the subarachnoid space has been demonstrated.^{2, 6} Unfortunately, the pedicle in the present case was ligated before its connection with the dura was severed and a communication with the subarachnoid space was not shown. Microscopically, the cyst wall is composed of avascular collagenous fibrous tissue and its inner surface is lined by a single layer of flattened epithelium similar to the arachnoid membrane. It thus seems to contain the elements common to both the dura and arachnoid.

The symptoms of spinal extradural cyst are largely those of any other tumor encroaching upon the cord and giving rise to signs of cord compression. Weakness and spasticity of one or both legs are usually the first symptoms to appear, which gradually progress into a severe spastic paraplegia. Pain is usually strikingly absent. This seems strange since most of the cysts arise from or near the exit of one of the posterior nerve roots. This seeming paradox is probably best explained by the nature of the tumor itself, the soft, easily adaptable encysted fluid causes very little irritation and hence gives rise to no irritative phenomena. The tracts lying in the dorsal column of the cord are usually severely affected. Loss of position and kinesthetic sense is the usual rule, whereas the epicritic sense is usually less seriously involved. Loss of sphincter control is rare, as one would expect from the location of the tumor in the thoracic region. Sphincter disturbances are late manifestations and usually indicate severe cord damage.

The striking features on examination are the signs that usually accompany cord compression and pyramidal tract involvement, *i. e.*, spastic paraplegia, hyperactive knee and ankle jerks, sustained clonus, and a positive Babinski sign. The deep sensibilities are severely impaired and the position-sense is usually absent. Cutaneous sensation to light touch, pin-prick, heat and cold is usually diminished below the segmental level of the lesion, but the changes are usually minimal unless the lesion is of long duration.

Lumbar puncture may or may not show a complete block. Even if the subarachnoid space is completely occluded, as pointed out by Cloward and Bucy,³ there may be a manometric rise on jugular compression due to the

pressure transmission quality of the fluid tumor. In these instances, however, lipiodol injection will demonstrate the block. The spinal fluid may be clear or xanthochromic, depending upon the completion and duration of the block. The total protein content of the spinal fluid is usually increased and in some instances may be quite high (200 mg per cent in the case herein reported).

In the roentgenograms the most striking changes are demonstrated. Changes within the neural arch are the earliest to appear and later manifest themselves in the bodies of the vertebrae. Elsberg, Dyke, and Brewer¹ focused attention on the broadening of the spinal canal at the site of the intraspinal lesion as measured by the transverse interpedicular diameter. The medial surfaces of the pedicles are flattened or concave and the thickness of the pedicles is greatly reduced. The overlying laminae are likewise thin and eroded. The bodies of the vertebrae in the lateral views, as was first demonstrated by Cloward,⁴ may show concavity of the posterior surfaces with broadening of the spinal canal. Other changes within the vertebral body characteristic of those seen in *kyphosis dorsalis juvenilis* are usually an accompaniment of these extradural cysts. The earliest change demonstrable is an erosion or rounding off of the anterior superior and anterior inferior corners of the vertebral bodies, as described by Scheurmann.⁶ As the process progresses the intervertebral disk may rupture into the bodies and the involved vertebrae may collapse anteriorly giving rise to a rounded kyphosis. Cloward and Bucy⁴ were the first to recognize that the changes occurring within the vertebral bodies in cases of extradural spinal cyst were identical with those occurring in *kyphosis dorsalis juvenilis*. They surmised that these vertebral changes were secondary to the presence of the intraspinal cyst, and advanced the hypothesis that the destruction of the vertebral body was the result of venous stasis caused by compression and occlusion of the venous channels draining these bodies. If this theory is correct, then it is reasonable to assume that this destructive process ceases to exist upon the removal of the cyst and that kyphosis if not present should not develop, and if it already exists its progress should be arrested provided adequate protection is given the spine during the period of reconstructive healing, either in the form of plaster jacket or spinal fusion. Further reports and observation of cases will prove or disprove this theory.

SUMMARY—A case of spinal extradural cyst, occurring in a 14-year-old Negro boy, is presented. The cyst, containing clear fluid and lined by flattened epithelium, arose from the dura by a thin pedicle near a posterior nerve root in the midthoracic region. It was accompanied by spastic paraplegia and was associated with erosion of the neural arches, broadening of the spinal canal, and changes within the vertebral bodies identical with those occurring in *kyphosis dorsalis juvenilis*. Complete recovery resulted from its operative removal. A brief discussion of the symptomatology and pathology is presented.

CONCLUSIONS

(1) Paraplegia in an adolescent, associated with broadening of the neural canal and erosion of the vertebral bodies in the midthoracic region, as described by Elsberg, Dyke, and Brewer,^{2,1} and Cloward and Bucy,³ is pathognomonic of spinal extradural cyst

(2) There is more evidence that spinal extradural cyst arises as a true meningeal diverticulum rather than as a herniation of the arachnoid through a defect in the dura

(3) The theory, advanced by Cloward and Bucy,³ that the destruction of the vertebral body results from venous stasis secondary to the presence of the intraspinal cyst appears to be tenable

(4) Excellent results can be expected from the early recognition and prompt operative removal of the cyst

REFERENCES

- ¹ Elsberg, C A, Dyke, C G, and Brewer, E D Symptoms and Diagnosis of Extradural Cysts Bull Neurol Inst New York, 3, 395-417, March, 1934
- ² Lehman, E P Spinal Extradural Cysts Am Jour Surg, 28, 307-322, May, 1935
- ³ Cloward, R B, and Bucy, P C Spinal Extradural Cyst and Kyphosis Dorsalis Juvenilis Am Jour Roentgenol, 38, 681-706, November, 1937
- ⁴ Cloward, R B Spinal Extradural Cysts ANNALS OF SURGERY, 105, 401-407, March, 1937
- ⁵ Kelly, T S B Nonparasitic Extradural Cyst of Spinal Canal Lancet, 2, 13-16, July 3, 1937
- ⁶ Quoted from Cloward and Bucy³

POSTOPERATIVE TEMPERATURE REACTIONS REDUCTIONS OBTAINED BY STERILIZING THE AIR WITH BACTERICIDAL RADIANT ENERGY*

SEASONAL VARIATIONS

DRYLL HART, M D

AND

S E UPCHURCH, M D

DURHAM, N C

FROM THE DEPARTMENT OF SURGERY, DUKE UNIVERSITY SCHOOL OF MEDICINE AND HOSPITAL, DURHAM, N C

WITH the introduction of sterilization of the air into our operating rooms, there was a striking improvement in postoperative results,^{1 2 3} namely

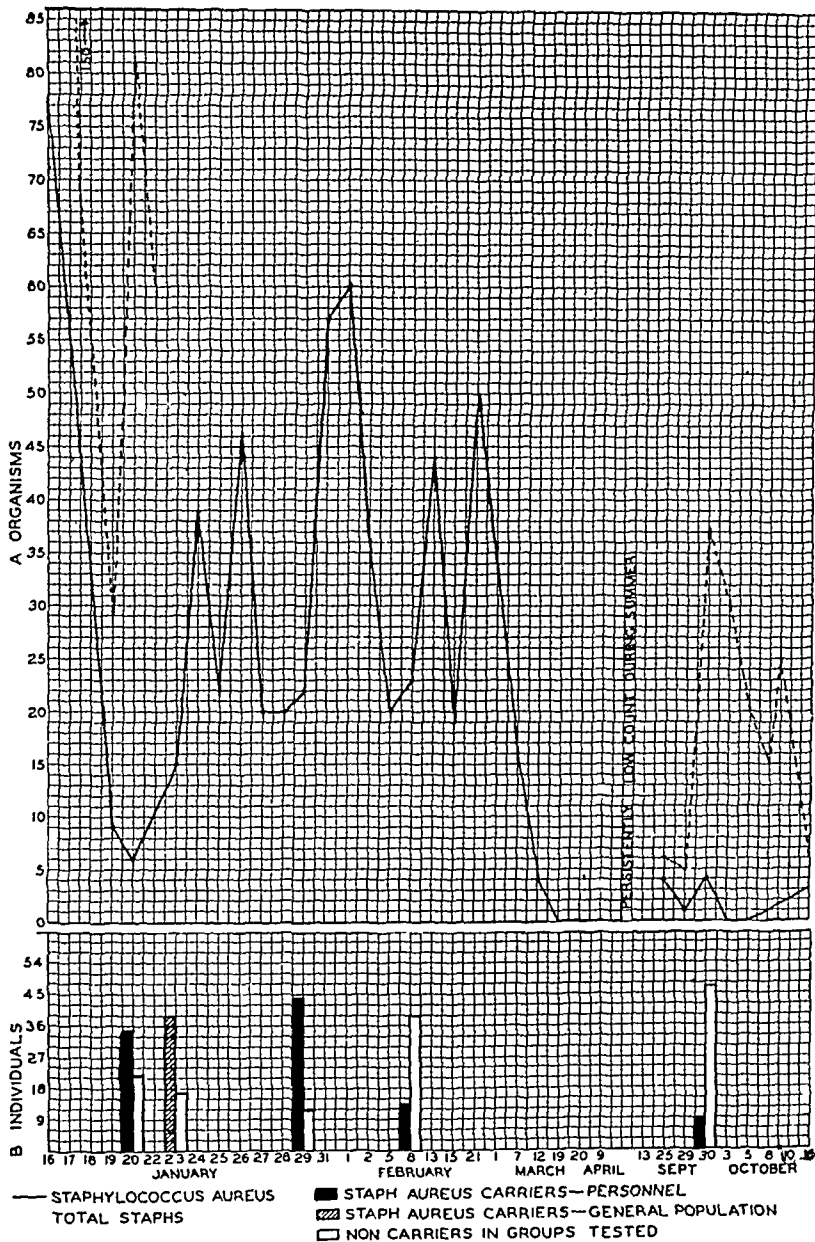
- (1) Lower postoperative temperature elevations
- (2) Shorter duration of postoperative temperature elevations
- (3) Reduction in the percentage of infections
- (4) Improved wound healing
- (5) Less severe systemic reactions

It was soon noted that during the warmer months this improvement in regard to the elevation of temperature and the duration of elevated temperature following operation was not so good as had been the case during the cooler months. An analysis of 132 individual stages of extrapleural thoracoplasty performed in a field of sterile air,⁴ showed that during the warmer months (May 15 to October 15) the number of patients running a postoperative temperature above 38° C (100.4° F) increased to 49 per cent as compared to 28 per cent for the cooler months (October 15 to May 15) while the number of patients running a temperature elevation (above 37.5° C [99.5° F] or the preoperative level) for more than four days after operation, increased to 43 per cent as compared to 13 per cent during the cooler months.⁴

Before beginning sterilization of the air, it had been our impression that the best postoperative reactions occurred during the warmer months, at which time we knew the bacterial contamination of the air was low. It has already been reported that, in our occupied operating rooms, the number of pathogenic or other bacteria floating in the air is greater during the cooler than during the warmer months^{2 5} (Charts 1 and 2). Therefore, large operative procedures of choice were postponed until such a time. Naturally, with sterilization of the air we obtained the greatest improvement in our results during those periods when the air contamination was highest. We were surprised, however, to find that under this new condition, even though our results were improved throughout the entire year, our greatest postoperative reactions now occurred during the summer, at which time we had formerly obtained our best results. It soon became evident that some factor other than air contamina-

* Read before the Southern Surgical Association, White Sulphur Springs, W Va, December 6, 7, 8, 1938

tion came into play during the warmer months and was the cause of the greater postoperative temperature reactions occurring then



operation or after the first few days following operation. It seems probable that perspiration may play an important rôle in washing organisms out of deeper, more protected parts of the skin, either by the normal flow or by massage and maceration of the wet skin, so that on a hot day the surface of the skin cannot be kept sterile for more than a few minutes (Fig 1). This increases the likelihood of wound contamination from the skin of either the patient or some member of the operating team. The most severe and the only extensive infection that we have had in over 400 clean primary incisions performed in a field of sterile air occurred in the first stage of an extrapleural thoracoplasty and resulted from a tear in the operator's glove on a very hot

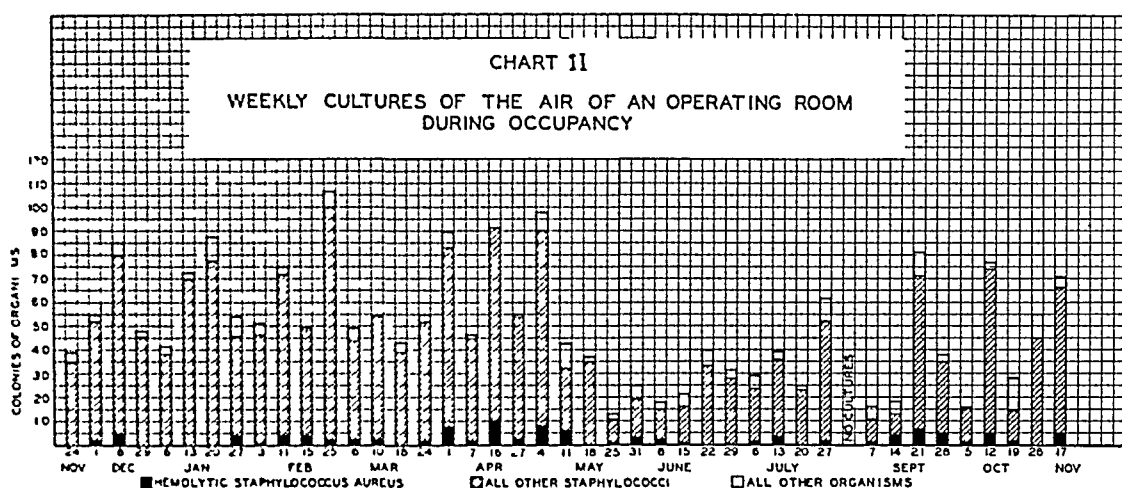


CHART 2—Weekly cultures of the air of an operating room during occupancy. The cultures were made by exposing a petri dish of blood agar to sedimentation from the air for one hour. After incubating the plates for 48 hours the colonies were identified and counted. Note the low total count and particularly the few hemolytic yellow Staphylococci during the warmer months. There was a close correlation between the intensity of the growth of these organisms in the noses and throats of the occupants of a room and the degree and type of bacterial contamination of the air in his room.

summer day. A large quantity of perspiration ran into the wound. Even though this was washed out immediately and as thoroughly as possible with sterile physiologic salt solution, the patient's temperature rose to 40° C within 24 hours, and the wound became extensively infected. The patient recovered following adequate drainage.

In order to obtain a more accurate evaluation of the seasonal variations in the postoperative reaction of the patient as indicated by the temperature elevation and its duration, we analyzed three groups of patients. Some of each group had been operated upon with and some without radiation of the air. The temperature charts were taken as an index of the postoperative reaction since the clinical thermometer is a highly accurate instrument and the records were made by a large number of nurses who had no idea that they were to be used other than as an accurate record of the patient's course. Nothing was left to the interpretation of the doctor who might be prejudiced in favor of air sterilization.

GROUP I—Extrapleural Thoracoplasties. These are taken since they are operations of great magnitude, with inevitable trauma, complete hemostasis

is difficult to obtain, it may not be possible to obliterate the dead space, and in our cases continuous catgut has been used for the buried sutures. The disadvantage of this type of case is that the temperature reaction may come from a stirring up, or an extension of the tuberculous process. However, this will usually be equalized in a large number of operations.

GROUP II—Inginal Herniorrhaphies. These are ideal in that they are clean incisions in otherwise healthy individuals. They are, however, small



FIG. 1.—Photographs of one of many series of 48 hour cultures of perspiration made from the skin of the hands of four members of the operating team (or operative region). The organisms are predominantly white *Staphylococci*. Cultures of the hands made immediately following their preparation for the operation showed no growth.

operative procedures and should show little reaction or infection even without sterilization of the air (in our hospital 3.6 per cent, all mild³). In this group of cases, since this was not a planned experiment, but a review of operations already performed, most of the larger herniae in obese individuals are in the group with radiation. A higher percentage of the smaller herniae, in which infection is less likely to occur, are in the group without radiation. This should be kept in mind in interpreting the charts since one would expect the greater postoperative reaction following the larger operation. Also in this group with radiation two of the highest reactions occurred in two children of one and

one-half and two years of age, who had then hernia repaired under ether anesthesia (Charts 4 A, 7 A, and 10 A—June and July) It is our impression that very young children operated upon under ether anesthesia frequently run a relatively high postoperative temperature

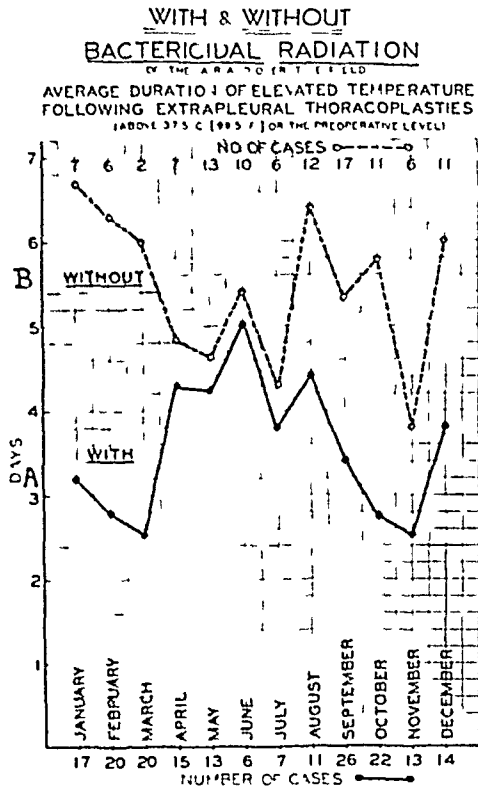


CHART 3

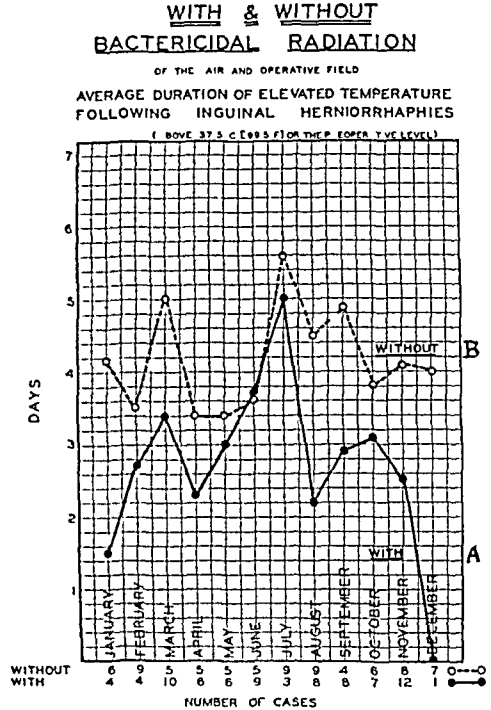


CHART 4

(CHART 3—Average duration of elevated temperature following extrapleural thoracotomies (recorded by month of operation) (A) With bactericidal radiation (B) Without bactericidal radiation

The following points should be noted in Charts 3, 4 and 5

(1) With bactericidal radiation there was a reduction in the average duration of elevated temperature throughout the entire year

(2) The reduction in the average duration of elevated temperature when the air was sterilized was greatest when the bacterial contamination was highest (Compare A with B and correlate with Charts 1 and 2)

(3) Without radiation the decrease in the average duration of postoperative temperature elevation during the warmer months was not as great as the drop in air contamination (Charts 1 and 2)

(4) With sterilization of the air the postoperative temperatures were of the longest average duration during the warmer months

(5) Paragraphs three and four above suggest that during the warmer months some condition other than air contamination enters the picture and causes the increased systemic temperature reaction. This condition may be the increase in the temperature and humidity of the surrounding air, but it seems more likely to be an increase in the wound contamination brought about by the bacteria in the perspiration resulting from this high temperature and humidity level

CHART 4—Average duration of elevated temperature following inguinal herniotomies (recorded by month of operation) (A) With bactericidal radiation (B) Without bactericidal radiation See legend appended to Chart 3 for points of special interest

Part of the higher average elevation and longer average duration of elevated temperature during June and July where radiation was used was caused by operations on two young children (one and a half years old for June and two years old for July), under ether anesthesia. Children of this age are more likely than adults to run a higher and longer temperature elevation following any operation under ether anesthesia. Part of the temperature reaction during February with radiation was caused by a postoperative parotitis

GROUP III—Radical Mastectomies These form a very poor group for study since the operation leaves the skin flaps with a poor blood supply. As a result, the skin may slough and secondary surface infection may follow. In addition to this, three of the cases in which radiation was used showed ulceration before operation. These three cases had a mild infection in the incision following operation and these alone accounted for three of the higher tempera-

tive recordings noted in Charts 5 A, 8 A and 11 A (February, March and October) Such ulcerated cases were ruled out in statistical analyses for postoperative wound infections in clean primary operative incisions both in

WITH & WITHOUT BACTERICIDAL RADIATION

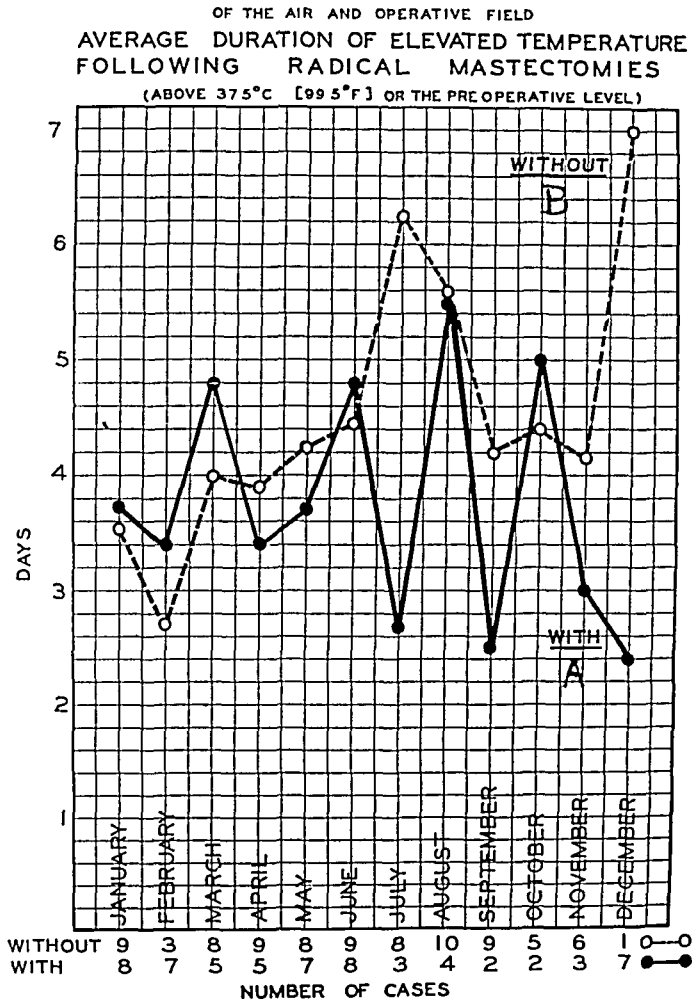


CHART 5—Average duration of elevated temperature following radical mastectomies (recorded by month of operation) (A) With bactericidal radiation (B) Without bactericidal radiation

Note that for three months February March and October, the average temperature duration each month was increased for the group with radiation by one mild wound infection resulting from an ulcerated infected tumor present at the time of operation. In curve B (without radiation) there was a very short average duration of elevated postoperative temperature during January February and March so this graph does not follow the curve shown in Chart 3. Radical mastectomy wounds are a poor selection for this study since, in addition to the cases showing ulceration before operation, the impaired blood supply in the large skin flaps may result in sloughing with the possibility of secondary, localized, superficial infection which may cause a low grade temperature reaction until healing is complete. Compare with Charts 3 and 4 and see legend appended to Chart 3 for points for special consideration.

the radiated and nonradiated groups. These ulcerated cases were, therefore, not included in previous reported statistics on operating room infections.

Each of the three groups of operations were divided into two series, one

including all operations performed in a field of sterile air and the other, all those performed without air sterilization *

For both series of each group, every operation was recorded in the month during which it was performed. Three charts were made of each series, so arranged as to compare the results in series A, where bactericidal radiation was used, with the results in series B, where radiation was not used. For both series in each group, the charting by months shows at a glance the variations dependent on the time of year and a comparison of A with B in each group shows the relative improvement brought about by radiation of the air during each month of the year.

The average duration of elevated temperature following operation is shown by months for

GROUP I	Extrapleural Thoracoplasties	{ A—with radiation B—without radiation }	Chart 3
GROUP II	Inguinal Herniorrhaphies	{ A—with radiation B—without radiation }	Chart 4
GROUP III	Radical Mastectomies	{ A—with radiation B—without radiation }	Chart 5

The maximum temperature elevation for every case (highest point at, or above which there are more than two recordings) expressed in percentages of the total number of such operations performed under similar conditions during the month is shown by months for

GROUP I	Extrapleural Thoracoplasties	{ A—with radiation B—without radiation }	Chart 6 A, B
GROUP II	Inguinal Herniorrhaphies	{ A—with radiation B—without radiation }	Chart 7 A, B
GROUP III	Radical Mastectomies	{ A—with radiation B—without radiation }	Chart 8 A, B

In these charts each case is placed in the division (37° – 37.5° , 37.6° – 38° , 38.1° – 38.5° , 38.6° – 39° and 39° + C) in which it falls. The number of cases in each division is then expressed as a percentage of the total number of cases for the given month to give Charts 6, 7 and 8.

Every recorded temperature for eight days following operation (taken at four-hour intervals when the patient is running any elevation, otherwise every

* If there was any difference in the general operating room technique it was less rigid where air sterilization was used than where it was not used. This is particularly true of the thoracoplasty and mastectomy groups and applied especially to skin sterilization, masking, number of visitors allowed, time selected for operation, and the duration of occupancy of the room before operation. The question of difference in masking has been raised frequently. Two large gauze masks each eight thicknesses of butter gauze were worn over the nose and mouth during many of the thoracoplasties without radiation, while only one was worn, without other covering, for most of the thoracoplasties with radiation.

WITH BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING EXTRAPLEURAL THORACOPLASTIES PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION

EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

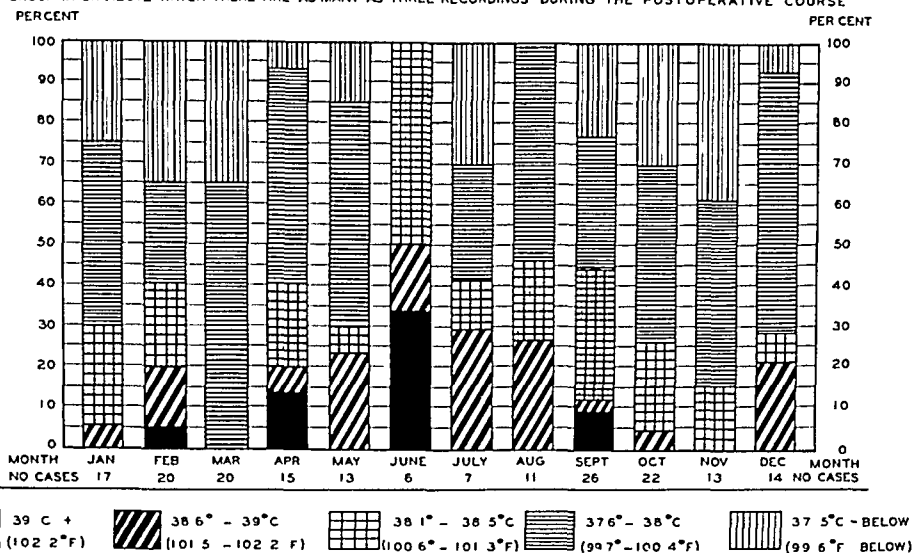


CHART 6A

WITHOUT BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING EXTRAPLEURAL THORACOPLASTIES PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION

EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

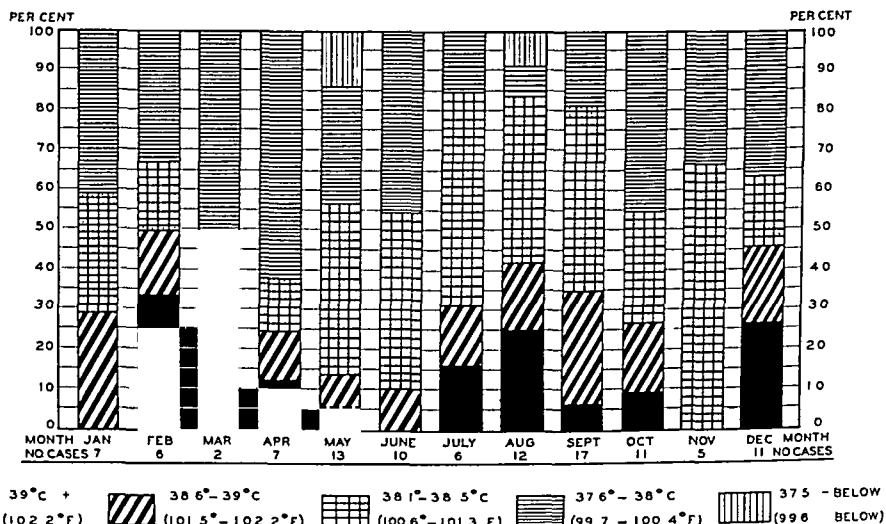


CHART 6B

CHART 6—Maximum temperature elevations following extrapleural thoracoplasties (A) With bactericidal radiation (B) Without bactericidal radiation. Each operation is placed in the month during which it was performed and in the highest temperature group (37°-37.5°, 37.6°-38°, 38.1°-38.5°, 38.6°-39°, 39.1°+C) in or above which there are as many as three recordings during the postoperative course. The number of cases in each temperature group is then expressed as a percentage of the total number of thoracoplasty operations performed during that month. This is done to facilitate comparisons, since the total for each month is 100 per cent regardless of the number of operations performed. The total number of cases on which the percentages are based is given beneath each month.

Special attention is called to the same five general points of interest in regard to the elevation of temperature in Charts 6, 7 and 8 as are given for the duration of temperature in the legend for Chart 3. (See legend for Chart 3 substituting average elevation for average duration of temperature.)

WITH BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING INGUINAL HERNIORRHAPHIES
PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION
EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE
GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

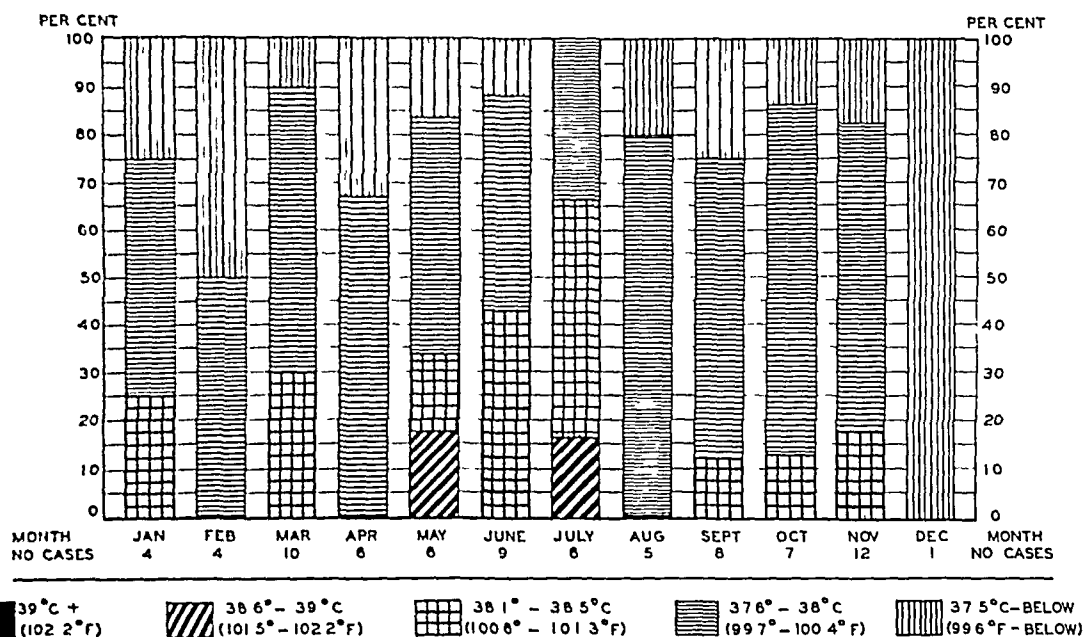


CHART 7A

WITHOUT BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING INGUINAL HERNIORRHAPHIES
PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION
EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE
GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

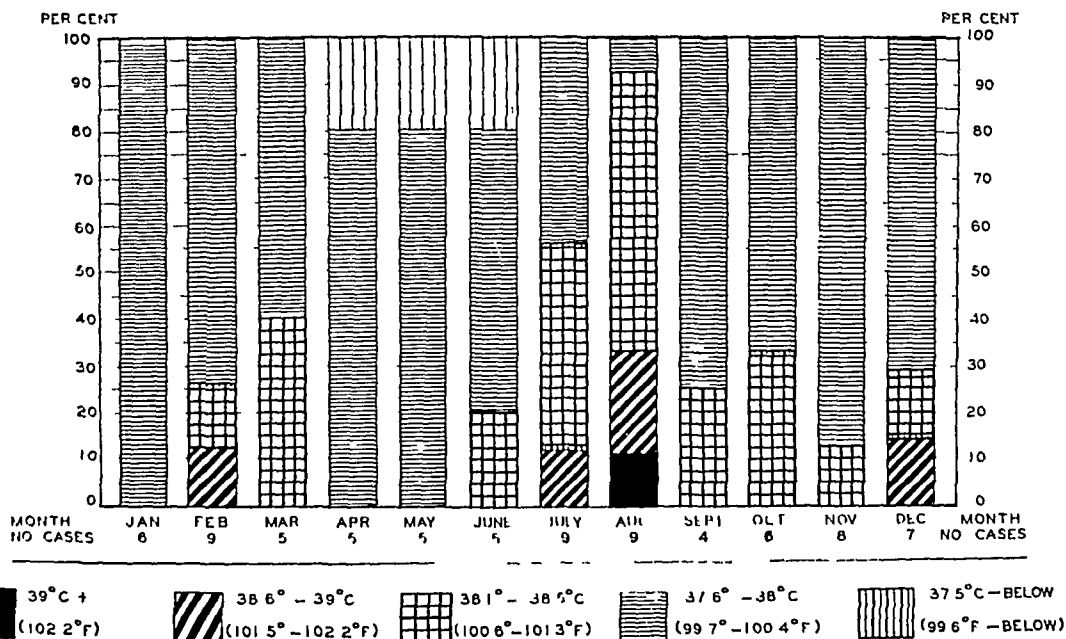


CHART 7B

CHART 7—Maximum temperature elevations following inguinal herniorrhaphies (A) With bactericidal radiation (B) Without bactericidal radiation

The method used in making the chart and the reason therefor are given in the legend for Chart 6. The special points for consideration in regard to the elevation of temperature are similar to those given for the duration of temperature elevation in the legend to Chart 3. See legend to Chart 4 for note about higher temperatures on two small children operated upon during June and July, and one patient with postoperative parotitis operated upon in February.

WITH BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING RADICAL MASTECTOMIES
PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION

EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

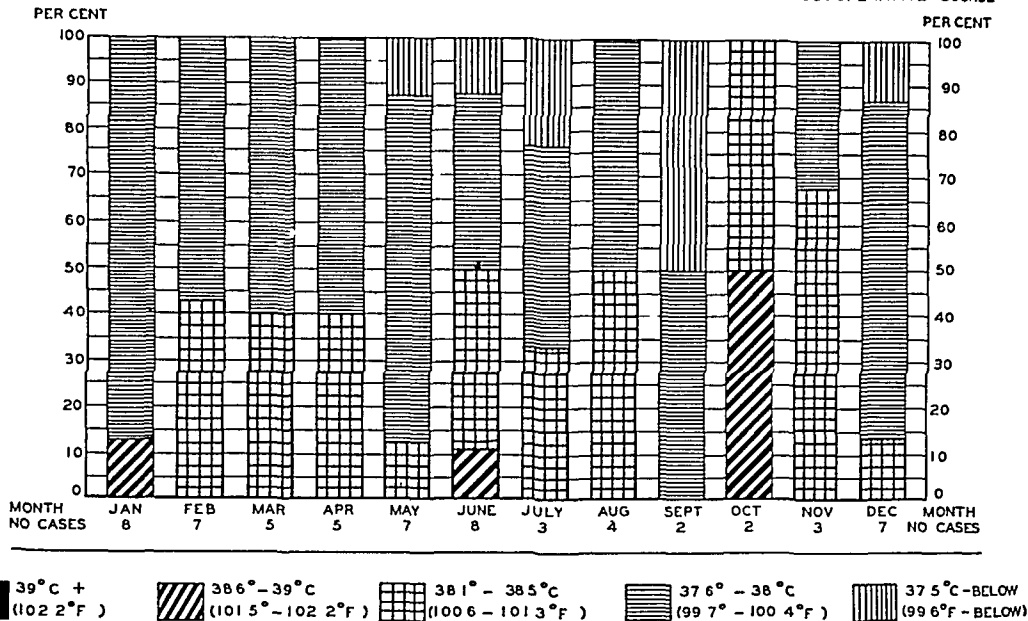


CHART 8A

WITHOUT BACTERICIDAL RADIATION

OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING RADICAL MASTECTOMIES
PERCENTAGES BASED ON THE HIGHEST TEMPERATURE FOR EACH OPERATION

EACH OPERATION IS PLACED IN THE MONTH DURING WHICH IT WAS PERFORMED AND IN THE HIGHEST TEMPERATURE GROUP IN OR ABOVE WHICH THERE ARE AS MANY AS THREE RECORDINGS DURING THE POSTOPERATIVE COURSE

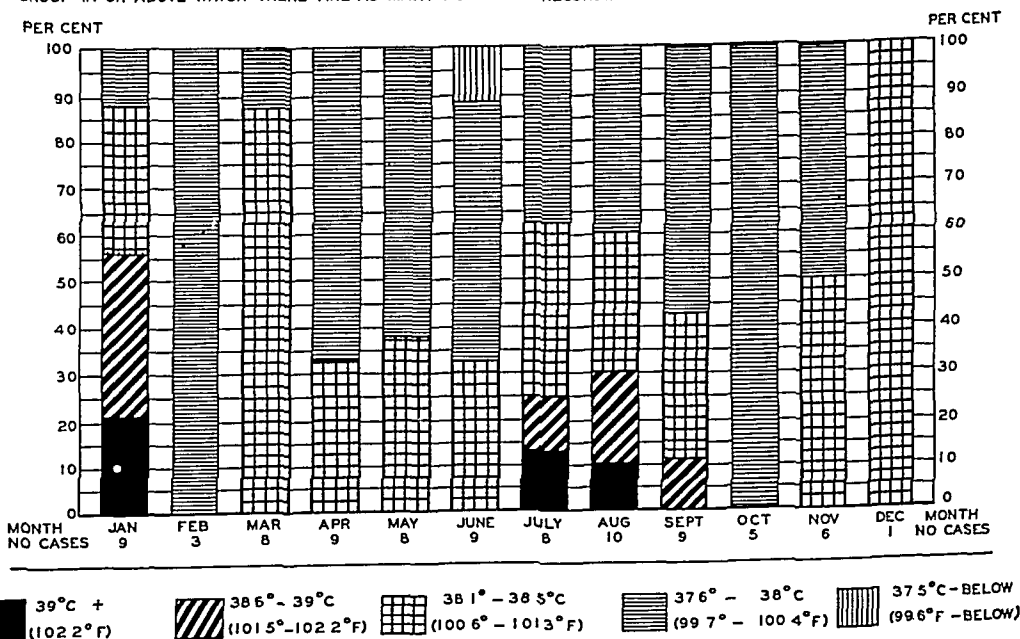


CHART 8B

CHART 8—Maximum temperature elevations following radical mastectomies (A) With bactericidal radiation (B) Without bactericidal radiation
The method used in making the chart and the reason therefor are given in the legend for Chart 6
The points for special consideration in regard to the elevation of temperature are similar to those given for the duration of the temperature elevation in the legends to Charts 3 and 5

four hours except at 12 midnight and 4 A M when the patient is sleeping) on every patient is shown by months for

GROUP I	Extrapleural Thoracoplasties	{ A—with radiation B—without radiation }	{ Chart 9 A, B }
GROUP II	Inguinal Herniorrhaphies	{ A—with radiation B—without radiation }	{ Chart 10 A, B }
GROUP III	Radical Mastectomies	{ A—with radiation B—without radiation }	{ Chart 11 A, B }

In preparing Charts 9, 10 and 11, every recorded temperature for eight days following operation was placed in the appropriate division (37° – 37.5° , 37.6° – 38° , 38.1° – 38.5° , 38.6° – 39° and 39° + C) and the total number of recordings in each division was then expressed as a percentage of the total such recordings for the given month. The total number of operations for each month is shown at the bottom of the charts.

EFFECT OF BACTERICIDAL RADIATION ON THE AIR

Without sterilization of the air, the average duration of the postoperative temperature elevation was longest when the air contamination was high and shortest when the air contamination was low. With sterilization of the air, there was a reduction in the average duration of elevated postoperative temperature roughly proportional to the degree of air contamination (compare A with B in Charts 3, 4 and 5 and correlate with Charts 1 and 2). There was a similar reduction in the average highest elevation of postoperative temperature (compare A with B in Charts 6, 7 and 8 and correlate with Charts 1 and 2), and in the height of the total temperature recordings for eight days following operations (compare A with B in Charts 9, 10 and 11 and correlate with Charts 1 and 2).

SEASONAL VARIATIONS IN THE POSTOPERATIVE TEMPERATURE REACTION

When bactericidal radiation was not used, the average duration of elevated temperature was definitely shorter during the earlier of the warmer months in extrapleural thoracoplasties, April through July, (Chart 3 B) and in inguinal herniorrhaphies, April through June, (Chart 4 B). Radical mastectomies (Chart 5 B) did not show such a drop since the curve was very low for January, February and March but it was also low during April, May and June as compared to July, August, and December. The charts showing the highest postoperative temperature elevations for each case (Charts 6 B, 7 B and 8 B) and those showing every temperature recording for eight days following operation (Charts 9 B, 10 B, and 11 B) have similar low recordings for the earlier warm months, April through June. All the charts (3 B through 11 B) showed a rise during the latter part of the warmer months.

With the introduction of sterilization of the air by bactericidal radiation, as noted above, there was little reduction in the temperature elevation and little shortening of the duration of elevation during these warmer months when

WITH

BACTERICIDAL RADIATION
OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING EXTRAPLEURAL THORACOPLASTIES
BASED ON EVERY RECORDED TEMPERATURE FOR THE FIRST
EIGHT POSTOPERATIVE DAYS

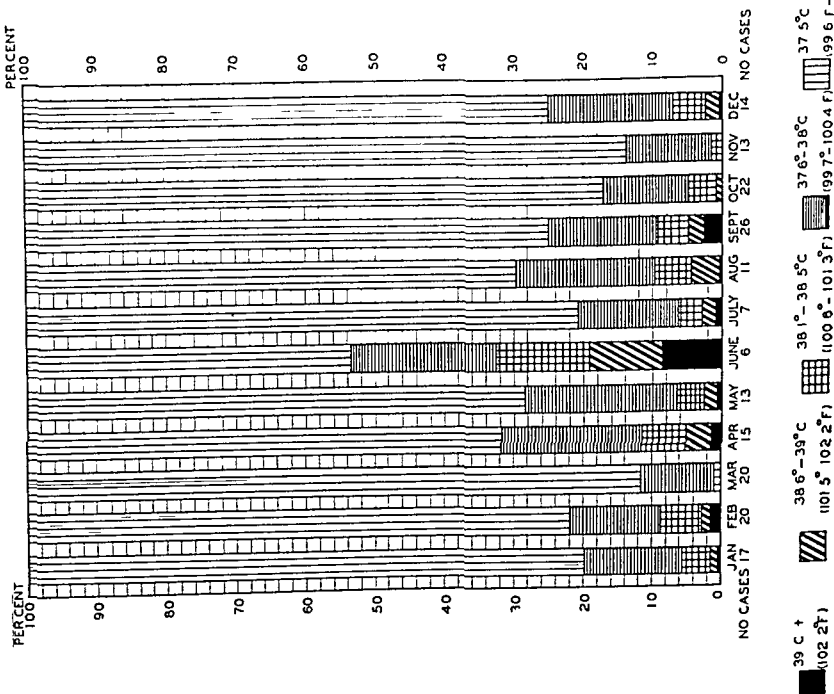


Chart 9A—Every recorded temperature for eight days following extrapleural thoracoplasties with bactericidal radiation

The percentages in this chart are based on every recorded temperature for eight days following operation (taken every four hours when the patient was running any elevation, otherwise, every four hours except at 12 midnight and 4 a.m. when sleeping). Every recorded temperature for eight days following operation was placed in the month during which the operation was performed and in the temperature group (37°-37.5°, 37.6°-38°, 38.1°-38.5°, 38.6°-39°, 39.1°+C) in which it fell. The number of recordings in each temperature group was then expressed as a percentage of the total recordings in all the temperature groups for that particular month. Compare with Chart 6 where the percentages are based on the highest level reached during the postoperative course. This chart naturally shows a much higher percentage of normal temperatures than Chart 6. It does not cover more than eight days, since most temperatures are down to normal in less than that time. To cover a longer period would increase the percentage of the lower and diminish the percentage of the higher temperature groups. Attention is called to the same points of special interest is given in the legends for Charts 3 and 6.

WITHOUT

BACTERICIDAL RADIATION
OF THE AIR AND OPERATIVE FIELD

TEMPERATURE ELEVATIONS FOLLOWING EXTRAPLEURAL THORACOPLASTIES
BASED ON EVERY RECORDED TEMPERATURE FOR THE FIRST
EIGHT POSTOPERATIVE DAYS

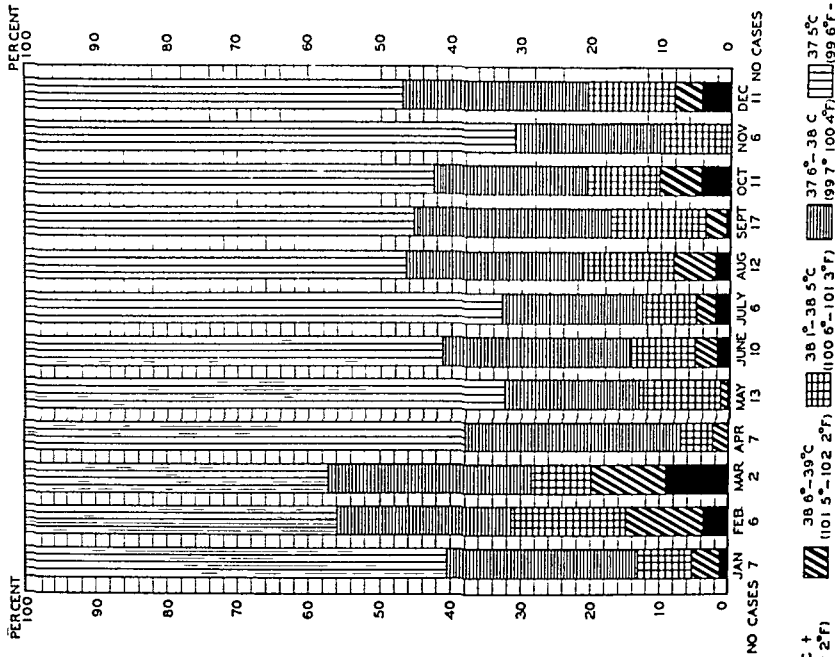


Chart 9B—Every recorded temperature for eight days following extrapleural thoracoplasties without bactericidal radiation

POSTOPERATIVE TEMPERATURE REACTIONS

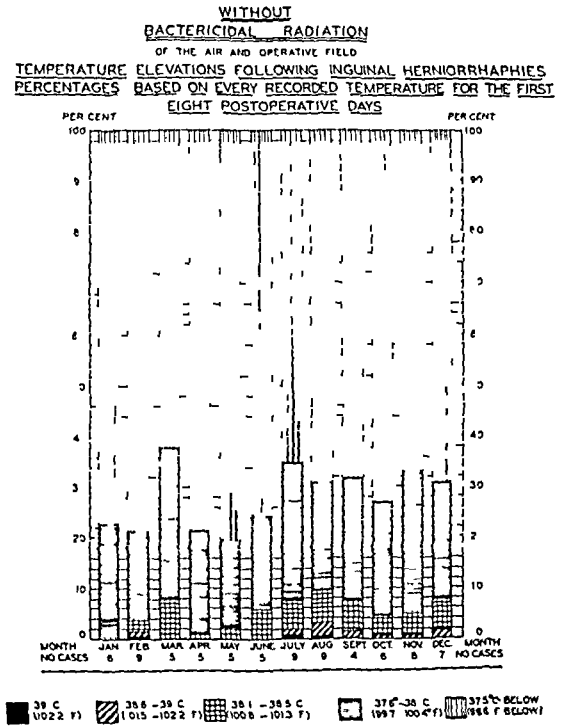
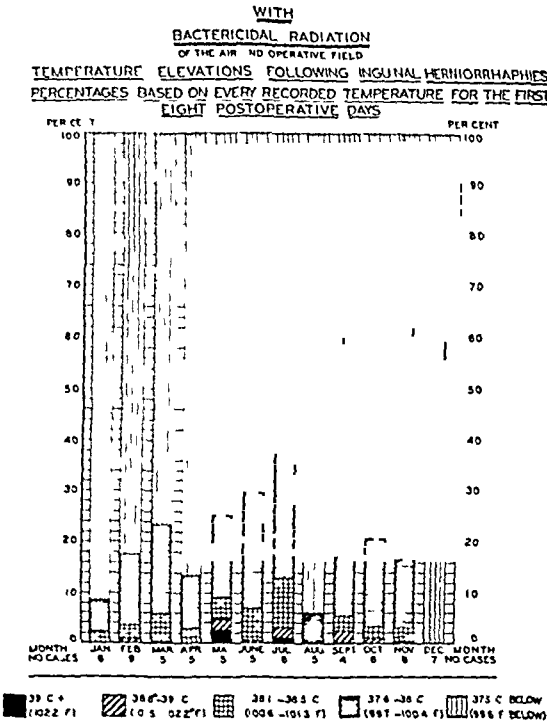


CHART 10—Every recorded temperature for eight days following inguinal herniorrhaphies (A) With bactericidal radiation (B) Without bactericidal radiation

The percentages are based on every recorded temperature for eight days following operation. See legend to Chart 9 for note as to how the chart was prepared and the reason therefor. This chart has the same relationship to Charts 4 and 7 that Chart 9 has to Charts 3 and 6. See legends to Charts 4 and 7, and the legend to Chart 3 for five points for special consideration.

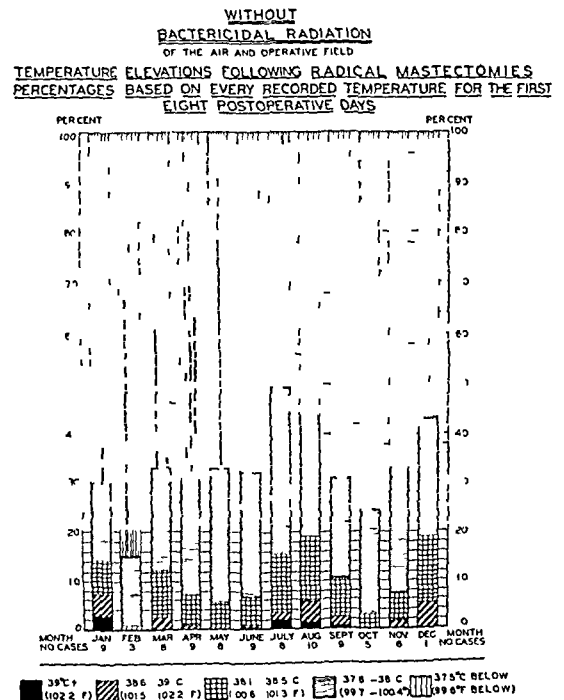
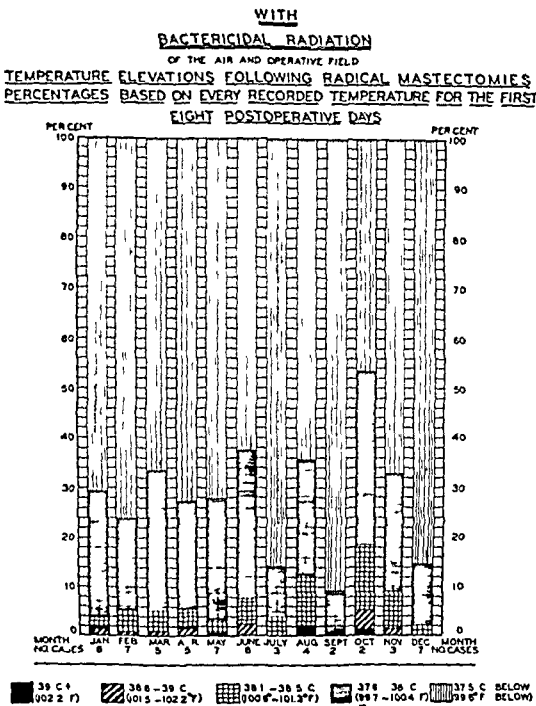


CHART 11—Every recorded temperature for eight days following radical mastectomies (A) With bactericidal radiation (B) Without bactericidal radiation

The percentages are based on every recorded temperature for eight days following operation. See legend to Chart 9 for note as to how the chart was prepared and the reason therefor. This chart has the same relationship to Charts 5 and 8 that Chart 9 has to Charts 3 and 6. See legends to Charts 5 and 8 and the legend to Chart 3 for five points for special consideration.

the air contamination is lowest. When the air is sterilized we have the highest and most prolonged temperature reactions during the warmer months. It can also be noted that where radiation was not used (B in Charts 3 through 11) the drop in the average duration of elevated temperature and average height of elevation was not as great as the drop in the amount of air contamination (compare A and B Charts 3 through 11 and correlate with Charts 1 and 2).

COMMENT—It seems to me that we have two conditions which vary with the time of year and that each has its effect on the postoperative temperature reaction. One of these is air contamination, which is quite variable with peaks and depressions throughout the year but in general is higher during the winter, may drop during April or May and begin to rise again from July to September or October (Charts 1 and 2). This contamination can, to a large extent, be overcome by sterilization of the air, and the results of this sterilization are seen by comparing A with B in the charts. The other condition is the temperature and humidity of the outside air, which may affect the patient directly by its influence on the dissipation of body heat or more indirectly by increasing perspiration, which facilitates the passage of bacteria out of the deeper layers of the skin, either directly by flow or indirectly by massage and maceration of the wet skin during the operative procedure. This contamination of the skin surface impairs our sterile technic and predisposes to wound contamination. In our section of the country, the general temperature and humidity of the air, with its resultant effect on the individual causing an increase in perspiration, reaches its peak during July and August, but may be of some significance from May through September. During April, May and June, the air contamination is usually low while the temperature and humidity are such that excessive perspiration is rare. Our best postoperative results without air sterilization occur during this period. During July and August, the air contamination is usually low but excessive perspiration is at its peak for the year. From April or May through July or August, we are less likely to obtain remarkable reductions in the postoperative temperature reactions by sterilization of the air, while during July and August, contaminated perspiration may cause an increase in the intensity of this reaction either with or without sterilization of the air. During September and October, with the cessation of excessive perspiration, there may be varying degrees of increase in the air contamination. In so far as this increasing air contamination causes an increase in the postoperative temperature reaction, we can obtain improvement by sterilization of the air. These general surgical principles, however, will in general be relatively stable with any operator working in the same operating room with a constant personnel. Local and general resistance of the patient may play an important part in the reaction in the wound and may vary widely with different individuals and with operations in different parts of the body. Particularly in the case of mastectomies, the local resistance may vary greatly as the result of variation in the amount of fat present and the blood supply available to all parts of the flaps. In certain cases without primary infection

sloughs develop in the skin flaps. Secondary infection is then inevitable and may cause slight but prolonged elevation of temperature. Three of the patients in the group of mastectomies with radiation had ulcerated lesions before operation, and following operation their wounds became mildly infected. Even though the ulcerated area was entirely covered during the operation, these patients ran a definitely increased risk of infection as a result of cutting across the lymphatics which drained the ulcerated area. These three infections accounted for three of the peaks of temperature elevation and duration where radiation was used (Charts 5 A, 8 A and 11 A—February, March and October). Children having a general anesthetic are more likely than adults to run a relatively high postoperative temperature elevation. This accounted for two of the higher temperature levels in hemorrhaphies performed with radiation (Charts 4 A, 7 A and 10 A—June and July).

SUMMARY —(1) In the well-run, modern operating room air contamination by pathogenic bacteria is the greatest source of danger of wound contamination as indicated not only by gross suppuration in the occasional case but by an increased local and systemic reaction in many patients whose wounds never show evidence of gross suppuration. Over 95 per cent of this danger of contamination from the air can be eliminated by sterilization of the air with bactericidal radiation.^{1 2 3 4}

(2) In the occupied operation room this air contamination is, in general, much lower during the warmer than during the cooler months.

(3) Without air sterilization the decrease in the postoperative reaction of the patient during the summer is not as great as the reduction in the air contamination with pathogenic bacteria.

(4) With the elimination of air contamination by sterilization, the postoperative reaction of the patient is greater during the warmer months than during the colder months.

(5) Three and four in the summary can be explained by the rôle which perspiration may play in producing wound contamination by washing bacteria out of the deeper layers of the skin during the operative procedure.

CONCLUSIONS

Before the introduction of antiseptic and aseptic surgery, contact contamination of operative wounds played by far the major rôle in operating room infections, so that despite the emphasis placed by Lister on the air as a source of danger it came to be ignored.

With the great reduction in contact contamination brought about by the development of aseptic surgery and the improved local resistance of the patient brought about by improved hemostasis and the development of relatively atraumatic surgery, operations of progressively increasing magnitude were performed. With the elimination of most of the contact transfers of large numbers of bacteria in operative procedures, the fewer bacteria floating in the air have assumed the place of major importance to-day. This same

method of transfer probably plays an important rôle in the spread of certain infectious diseases, particularly those affecting the respiratory passages.^{6, 7} In the small incisions made in individuals in vigorous health with minimal trauma, good hemostasis, nonirritating sutures and ligatures, and located in healthy tissue where dead space can be obliterated and the part kept at rest during the early stages of healing, the few mildly pathogenic organisms entering from the air will very rarely cause suppuration. As we diverge from these more or less ideal conditions and operate upon the patient who has less general resistance, carrying our larger procedures in which a greater amount of trauma is inevitable, in which complete hemostasis is difficult to obtain, at times in tissues of lowered resistance, possibly with dead space which cannot be obliterated or parts which cannot be immobilized or with the use of catgut which may at times be indicated, occasionally with the necessity of inserting drains, and during epidemics of respiratory infections when not only may the number of bacteria but the pathogenicity of the bacteria in the air be increased, the dangers of the wound's becoming infected with organisms dropping out of the air becomes progressively greater. Under any given conditions the local and systemic reaction of the patient is greater when more virulent organisms in larger numbers enter the wound.

With the elimination of the air as a source of wound contamination, perspiration assumes a position of major importance. By continuously washing bacteria out of the protected deeper layers of the skin it prevents the maintenance of sterility on the surface of the skin of the patient which may at times be exposed in the operative field, contaminates the sterile gowns of the team, and accumulates, in quantity, in the rubber gloves from which it may be expressed into the wound if an accidental puncture occurs. Perspiration may thus help account for the fact that in the summer months there is a greater postoperative temperature reaction than would be expected with the low air contamination. Likewise, the results obtained by sterilization of the air are not as striking during the warmer months as they are during the cooler part of the year when the air contamination is greater.

Air conditioning with the elimination of perspiration may bring us another step nearer that probably unattainable ideal of operating without the entrance of any bacteria into the wound.

REFERENCES

- ¹ Hart, Deryl. Sterilization of the Air in the Operating Room by Special Bactericidal Radiant Energy. *Jour Thorac Surg*, 6, No 1, 45, October, 1936.
- ² Hart, Deryl. Operation Room Infections, Control of Air-Borne Pathogenic Organisms, with Particular Reference to the Use of Special Bactericidal Radiant Energy, Preliminary Report. *Arch Surg*, 34, No 5, 874, May, 1937.
- ³ Hart, Deryl. Sterilization of the Air in the Operating Room by Bactericidal Radiant Energy. Results in Over 800 Operations. *Arch Surg*. In press.
- ⁴ Hart, Deryl. Sterilization of the Air in the Operating Room with Bactericidal Radiation. *Jour Thorac Surg*, 7, No 5, 525-535, June, 1938.
- ⁵ Hart, Deryl, and Schiebel, H. M. Rôle of the Respiratory Tract in Air Contamination. A Comparative Study of the Bacterial Flora of the Air of a Room with the Flora

in the Nasopharynx of Its Occupants Correlation with Contamination of the Air in the Operating Room Arch Surg In press

⁶ Wells, W F, and Wells, M W Air-Borne Infections J A M A, 107, 1699, 1936

⁷ Wells, W F, and Wells, M W Air-Borne Infection J A M A, 107, 1805, 1936

DISCUSSION—DR REGINALD H JACKSON (Madison, Wis) History, I am sure, will record an ever increasing debt of gratitude to Hart and his colleagues for their pioneer work in calling attention to the hitherto generally overlooked fact that entirely aside from the long-recognized sources of clinical wound infection, such as imperfect sterilization of instruments, ligatures, gloves, *etc*, there exists a most potent direct source of wound contamination and infection in the air of the operating room, one which strikes with a frequency and viciousness in direct relation to First, the number of human beings in the room and, second, the time of the year, the peak of clinical wound infections synchronizing with the peak of upper respiratory infections of humans

All surgeons, without exception, must be aroused to a renewed interest in this subject Though the scientific investigations of Hart, Ives, and Hirschfield, J Staige Davis and others, the following statements may be accepted as unequivocally true

(1) That practically all operating rooms contain, in the air, on the floors, walls and ceilings, more Staphylococci and, at times, hemolytic Streptococci, than any other department in the hospital except the nose and throat department

(2) The *Staphylococcus aureus* is the principal and general source of infection of clinical wounds

(3) These infecting agents gain direct entrance to the wound by precipitation from the air overlying the wounds, and by droplet infection

(4) Every wound made by the surgeon is contaminated and potentially infected in direct proportion to its size and the length of time of its exposure

(5) There are nearly always in the room, carriers of *Staphylococcus aureus* or hemolytic Streptococcus

(6) The surgeon himself may unwittingly be a carrier

(7) A run of such cases always means that the air of the room contains (as proved by culture) a higher percentage of these organisms than normally

(8) While the average incidence of such baleful clinical wound infections is from 4 to 6 per cent (heretofore recognized as an irreducible minimum), it at times rises to 18 to 20 per cent

(9) A scientific bacteriologic check-up on every link in the so-called aseptic chain may achieve a 100 per cent credit, and yet the incidence of clinical wound infections continues at two to three times the average

Certainly we all know that it is within the power of the surgeon to change a contaminated, potentially infected traumatic wound into a clean one which will generally heal per primam, through débridement and thorough cleansing with soap Why—in view of the fact that nearly every wound made by the surgeon may be proved to be contaminated with Staphylococci from the air—should we not apply the same “debacterializing” method? Objections on the basis that it would be a messy, unsurgical and unnecessary procedure that would violate the great surgical principle of keeping the wound as dry as possible, and would militate against ideal wound repair, are annihilated by actual trial of the method in over 200 instances, proving that instead of militating against primary union, it actually insures ideal wound repair and lowers the incidence of clinical wound infection practically to the vanishing point

There will always be instances of secondary wound infection, as uncontrollable factors are involved entirely aside from the presence of bacteria in the wound. Whether the "debacterIALIZATION" of a clinical wound is accomplished before closure by this method or by the Hart method is immaterial, I am convinced that surgeons should and will use one or the other until something better offers. We have been hypnotized too long by the phrase "the aseptic chain technic," overlooking the factor of direct air contamination which Hart and others are again calling to our attention. Any surgeon who doubts the verity of these contentions may, and should, repeat the tests under the supervision of a bacteriologist and forever be disabused of the idea that it is all nonsense.

DR. WALTMAN WALTERS (Rochester, Minn.) It seems to me that this epochal study, clinically as well as experimentally, deserves more consideration by this Society as well as by other surgical societies than has resulted to date. It carries a great deal of economic as well as medico-legal significance. I would like to see this topic chosen for presentation at a symposium at the next meeting of this Society. To change the set-up in operating rooms throughout the country will entail considerable expense, which must be borne by the patient in the long run. It will be interesting to note the results which other surgeons obtain in closed, irradiated operating rooms.

At the Mayo Clinic, we are able to obtain consent for postmortem examination in approximately 90 per cent of cases. For 14 years I have studied the causes of death after operations on the biliary tract and stomach, and the outstanding thing has been the infrequency with which infection of wounds or intraperitoneal infection has played a part unless there was an associated toxemia or debility or unless a severely infected lesion was being operated upon. In the cases which I studied, the failure to recover after surgical procedures was caused principally by pulmonary complications such as infection, infarcts or embolism.

Doctor Hart stated that, in the late summer months, when perspiration is more active than at other times, the incidence of infections increases. Might that not be a matter of lowered resistance of the patients after passing through extremely hot weather, in which we know the physiologic resistance of the patient as well as of the doctor is reduced, rather than an increase in the frequency or virulence of the infection? Doctor Hart has stated, I believe, that the temperature and pulse rate indicate the degree of infection. Might it not be that infections in other parts of the body, in the respiratory tract and urinary tract particularly, which frequently occur immediately after operation, are partly responsible for fever or increase of pulse rate?

There is another factor in the study which I think deserves consideration. What is the effect of such irradiation in a closed operating room over long periods each day on the people who work in that room, such as the nurses, interns, anesthetists and the surgeons? We are studying the effect of a strong light used in the operating field on fatigue of the eyes of the surgeon and assistants. There are many possibilities for studying the effects of the performance of surgical procedures on the surgical team itself, such as the effects on the surgeon's blood pressure after two or three operations have been carried out, the fatigue of the eyes, muscles and nerves, and so forth. Has Doctor Hart studied these questions in relation to irradiation of the operating room as far as the personnel of the operating room is concerned? That, it seems to me, should be an important part of the study. If this method of sterilization of the surgical field plays a rôle in the reduction of incidence of infection, we must be prepared to withstand criticism for failure to use it,

if infections of wounds should develop. I hope that there will be some surgeons who also will study this problem from the points of view of the set-up of operating rooms in general use to-day.

DR ISADORE COHN (New Orleans, La.) There are two or three thoughts which have occurred to me, and I believe many of them could be answered very definitely almost by a rising vote. Do the members of this Society have, generally, so large a percentage of wound infections, not under irradiated conditions? The men who are operating in smaller towns have to consider the expense of introducing this apparatus. I believe further, that if we sincerely feel this is an essential thing, is it not our duty when we get home to insist that hospitals do this? Are we going to revert to the time of Lister and his carbolic spray?

I think Doctor Walters' suggestion of a symposium is an excellent thing. I wonder if there is not some possibility of a lawyer taking a case for somebody with a burn which they might say might be accounted for by irradiation.

DR FRANK SIRICKLER (Louisville, Ky.) As I see it, this question simmers down to two propositions. We can sterilize the operating room, the dressings, the instruments but we still have the patient to consider. We all know that we have foci of infection in the gallbladder, teeth, tonsils, intestinal tract, *etc*. The problem is, if we sterilize all these other agencies, how are we going to sterilize the patient? If we make a wound and he has a lot of bacteria circulating in the blood stream he is likely to develop infection, and I do not believe we can ever overcome that. Up in Kentucky we do not have so many infections. Once or twice I have inadvertently punctured a glove, and the patient got well without infection. I do not understand why we get so many infections in certain parts of the country. Maybe we are careless and do not watch things so well, but the patients heal up all right. There are many angles to be considered.

DR DERYL HART (Durham, N. C., in closing) I agree with what Doctor Jackson has said, and I think that washing out the wound is a valuable procedure. We have followed this technic for many years and find that it washes out much debris, particularly loose particles of fat, coagulated serum, and blood. Before beginning sterilization of the air we washed out all large wounds very thoroughly, but were disappointed in that we could not eliminate the occasional infections by such a technic. I want to emphasize again that I think it would be a great detriment to surgery if, for any reason, we should give up any of the generally accepted practices of good surgery such as sterility, avoidance of trauma, meticulous hemostasis, obliteration of dead space, avoidance of irritating sutures or drains where possible, immobilization of the wound, *etc*. Sterilization of the air attacks only one source of infection—the air—highly contaminated probably because of the inadequacy of our operating room masks. Organisms on the skin, or if by chance in the blood stream, or those introduced by contact contamination, may not be affected by air sterilization, so we must maintain our best surgical technic, and cannot assume that the wound is free of bacteria even if the air is completely sterilized.

Again may we emphasize that our principal objective has been to prove the importance of the air as a source of wound contamination. Bactericidal radiation was adopted as the only practical means of sterilizing the air in order to prove the importance of this source of contamination by its elimination. The results given in this paper, in our opinion, prove that the contamination in the air of our operating rooms is at the present time the greatest source of danger of wound infection in clean operations.

In reply to Doctor Walters, we can say that so long as the law requires that "a man have the skill and use the precautions such as are accepted by the profession in the community where he works" he will have no need to fear the lawyers. Until sterilization of the air is more universally accepted as part of the operating room technic, no lawyer will have a case even though it could be proved that the infection came from the air. For the patient or his lawyer to prove that any specific infection came from a definite source would be all but impossible. If the time comes when sterile air is generally accepted as a requirement of good operating room technic, the lawyer then may have a case. In the meantime, for the doctor who is convinced that most of his infections come from the air, his conscience may be more annoying than his patient's lawyer.

In reply to the question of expense making the use of bactericidal radiation prohibitive, these tubes now retail for \$10.00 each, so the cost of equipping a room is probably less than the cost of a good operating room light. They consume only about 10 watts of current per tube and our tubes, that have been in use for over two years, show less than 10 per cent depreciation in output of bactericidal radiation.

In regard to the type of operations in which the air should be sterilized, we do not consider it imperative in small incisions. For arthroplasties, extra-pleural thoracoplasties, radical mastectomies, large ventral herniae in obese patients, *etc.*, we feel it is indispensable. As time goes on, probably we will not be content with compromise in our sterile technic, regardless of the small size of the operation or the presence of other possible sources of contamination.

We do not believe that all the postoperative temperature elevation comes from the patient's reaction to bacteria in the wound, but after two and one-half years' experience in eliminating the bacteria from the air we are convinced that they play a major rôle in its production.

The question of eye fatigue has been raised. There would be no fatigue from the radiation itself, since the ray is invisible. However, it is necessary to protect the eyes by glasses or goggles and unless these are optically satisfactory they might cause symptoms. The radiation does not penetrate plain glass to any appreciable degree, but a high grade of pyrex glass may transmit a small percentage. We have made some blood studies on individuals working in a field of bactericidal radiation but have been unable to detect any change.

In regard to our "high percentage of infections" without bactericidal radiation, we feel that our rate of 4 per cent (exclusive of thoracoplasties) is about as low as we can expect.

Doctor Strickler made the statement that "we cannot sterilize the patient in one way and do not want to sterilize him in another." We make no claim that this radiation will kill the bacteria on the skin, since they might be protected in the crevices, and would never expect any effect on the bacteria within the body or its epithelial lined spaces. However, since this ray has very little penetrating power, we can at least feel assured that there is no danger of sterilizing the patient in any other way.

As already stated, I see no immediate or remote prospect of eliminating every source of wound contamination, such as from the skin or blood stream of the patient. This, however, should not deter us from eliminating a known source that in our opinion is of far greater importance.

BRIEF COMMUNICATIONS AND CASE REPORTS

AN ARTIFICIAL ANUS WITH MECHANICAL SPHINCTER

JOHANNES F S ESSER, M D

MONACO

THE operation to be described was designed to afford a method of voluntarily controlling the fecal discharge from a permanent colostomy

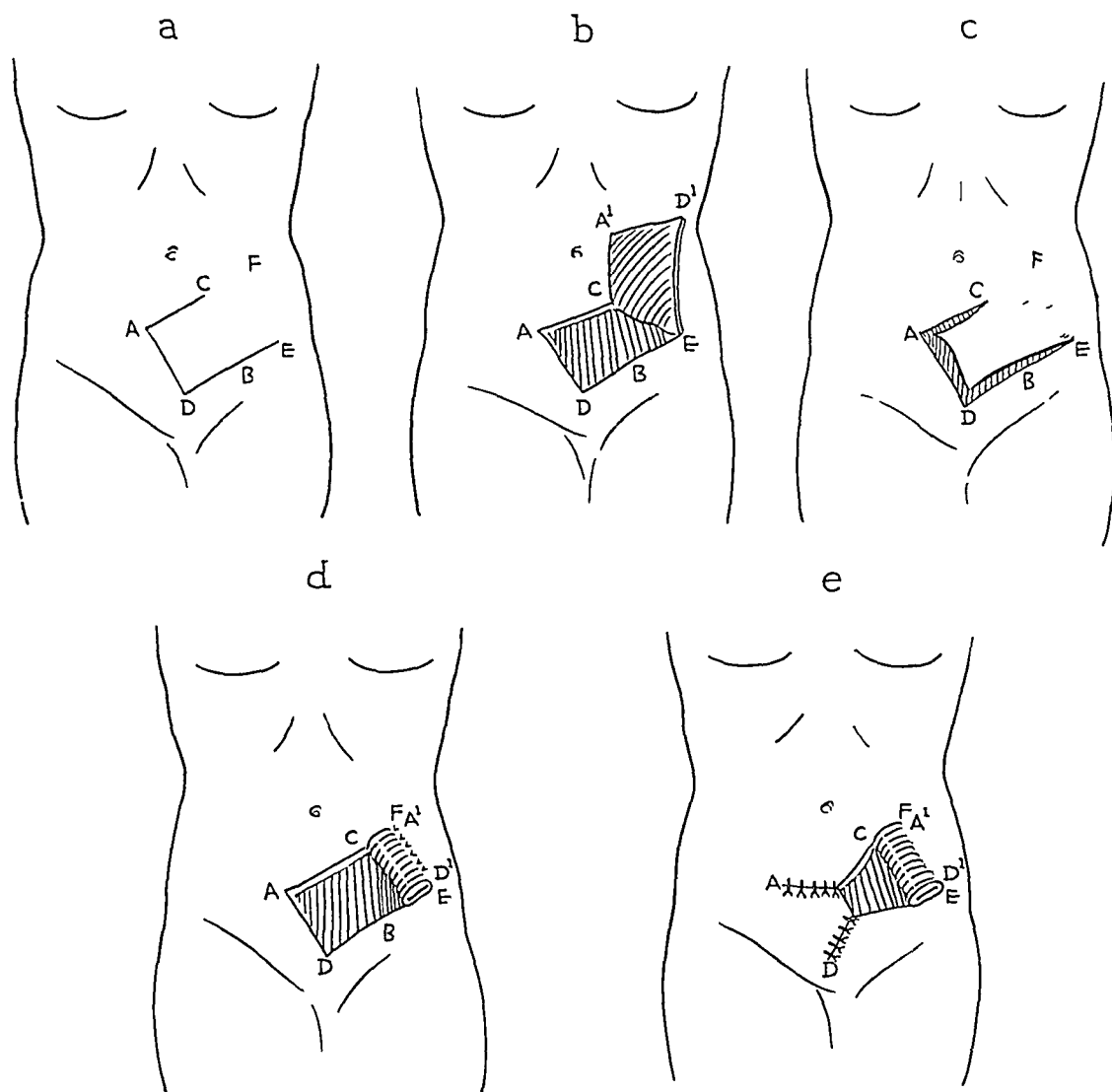


FIG 1—(a) Shows the outline of the incision employed (CADE) (b) Shows the skin flap is reflected laterally (c) Shows the freed skin flap ACDE, the skin of the part CFE being only loosened (d) Shows the protruding, proximal end of the intestine wrapped in the skin flap (e) Shows the edges of the denuded area approximated by longitudinal sutures

Operative Technique—A skin flap, CADE, is outlined and raised from the underlying tissues, the skin of the area CFE being merely separated from



FIG 2 (Case 1)—Shows the application of a spring clamp to the base of the skin tube containing the intestine



FIG 3 (Case 2)—Shows the final result. The irregularly scarred triangular area is the site of the epithelial inlay graft. Pincers have been introduced into the orifice of the intestinal segment.

the underlying tissues. The flap is turned laterally on its pedicle CE. The opening into the peritoneal cavity is made between points C and F underneath the skin flap while the flap is retracted upward to its utmost limit at points D' and A'.

The loop of the colon which is to form the colostomy is withdrawn. The bowel is severed and the proximal segment with its distal end temporarily clamped, is wrapped in the skin flap which is now directed downward.

The point D' of the skin flap is sewn by means of a metal suture to point E. The colon emerges from this opening. Interrupted metal sutures are then employed to anchor the border A'D' of the skin tube, containing the colon, to the line FE.

In order to partially obliterate the defect caused by raising the flap, traction is applied to the skin at the angle A by means of a simple hook, and the skin borders AC and AD are sutured as far as possible without causing excessive tension. In the same way traction is applied at the angle D and the skin borders DA and DE sutured. The area still denuded of skin is covered with an epithelial inlay (Essei). The inlay consists of a thin free skin graft placed upon a mold of stent-mass which has been fashioned to fit the defect accurately. The graft may be taken from the thigh or from the inner aspect of the arm. By applying firm pressure to the mold for seven days, the accumulation of secretion beneath the graft is prevented and healing is insured. The secondary defects are dressed with dry or vaselined gauze.

The clamp is then removed from the cut end of the bowel and the circular margins of bowel and skin tube approximated by means of interrupted metal sutures.

The new anus remains open and functions directly after the operation, the surrounding skin and sutures being protected by zinc ointment. The epithelial inlay pressing on the wound prevents fecal contamination.

Adequate nourishment of the extraperitoneal intestinal segment is insured by the vascular anastomoses which occur between the subcutaneous vessels of the skin tube and the vessels of the serosa of the bowel, as well as by the vessels severed at the cut end of the bowel. Because of the rich circulation of the skin tube, derived from its wide pedicle, a spring metal clamp may be applied to the tube after one month without fear of embarrassing the circulation of the bowel.

AN ELECTROSURGICAL OPERATION FOR EXCISION OF AN HYDROCELE SAC

LOUIS T WRIGHT, M D

NEW YORK, N Y

AND SAM A LOEB, M D

SWEETWATER, TEXAS

FROM THE SURGICAL SERVICE, MARION HOSPITAL, NEW YORK N Y LOUIS T WRIGHT M D, DIRECTOR

ELECTROSURGERY has not to our knowledge been used as an aid in hydrocele operations, and for this reason it is the purpose of this paper to record briefly our experience with the Bovie electrosurgical unit in the treatment of hydrocele. Massive postoperative hematoma is a most serious complication that occasionally follows hydrocele operations. Especially is this most likely to occur in large hydroceles with thick-walled sacs. An active hemorrhage after operation may necessitate a second operation to remove the blood clot and stop the bleeding. The Andrews tunica vaginalis eversion operation—the so-called “bottle operation”—is more frequently followed by recurrence of the hydrocele than the Winkelman sac-excision operation, although postoperative hemorrhage is more frequent after the latter. An infected, large, postoperative hematoma causes the patient great distress, though it, fortunately, is an unusual complication.

We began to use electrosurgery with the idea of reducing the incidence of postoperative hemorrhage and hydrocele recurrence. In the present series of 12 cases, it proved to be a simple, safe and easy method of excision of the tunica vaginalis and was totally devoid of complications.

Technic of Procedure—The left hand of the operator gently grasps the posterior surface of the scrotum, and the skin over the anterior surface of the hydrocele is stretched until it is taut. An anterior vertical incision, of necessary length, is made a few centimeters from the median raphe, with the cutting Bovie current, through the skin and all of the fascial and muscular layers down to, but not including the tunica vaginalis, if it can be avoided (Fig 1). Occasionally, we opened the sac by our incision, although it was not particularly desired, because it is much easier to free an unopened sac from the surrounding tissues than one that has been evacuated. If the sac has not been opened, it is gently stripped from its covering layers, and its contents are aspirated with a trocar. The sac is then opened and excised, with the cutting Bovie current, to within 1 or 1.5 cm of its attachment to the visceral layer of the tunica vaginalis (Fig 2). Bleeding points are caught with mosquito clamps, and all oozing is controlled with the coagulating current. The skin and fascial layers are included in the interrupted, vertical mattress sutures of silk, that close the wound. Dry sterile dressings are applied and the scrotum is supported by means of an adhesive plaster bridge.

Submitted for publication May 27, 1938

ILLUSTRATIVE CASE REPORTS

Case 1—Male, age 25 gave a history of trauma to the scrotum several months before admission to the hospital. Five days before admission 800 cc of light amber-colored fluid was aspirated. On admission a globular mass, 7 x 12 cm., was present in



FIG 1—Shows the electrode in place. Scissors separating the hypertrophied fibers of the cremasteric muscle and infundibuli form fascia from the tunica vaginalis. Marked hypertrophy of the cremasteric muscles is a common finding in large hydroceles of long standing although rarely mentioned. In this drawing it is too prominent.



FIG 2—Shows the tunica vaginalis opened and the line of sac excision.

the left side of the scrotum. It was not tender and trans-illuminated. The sac was excised, under spinal anesthesia, and the wound sutured without drainage. He was discharged eight days after the operation as cured.

Case 2—Male, age 34, complained of a left-sided scrotal mass that had been present for "some time." Examination showed a nonpainful cystic mass, 10 x 12 cm, which transilluminated. The operative wound healed by primary intention.

Case 3—Male, age 68, states that he has had a mass in the right side of his scrotum for years. Examination showed a large, nonpainful cystic mass in the right side of the scrotum, 10 x 12 cm, which transilluminated. The hydrocele sac was excised under local anesthesia. The wound healed by primary intention, except for a small slough at its lower angle.

Case 4—Male, age 38, who had noted a mass in the right side of his scrotum for some months. On examination, it was not tender, 5 x 6 cm. Under spinal anesthesia, the sac was excised and the wound healed per primam, except for a very slight skin slough at its lower angle.

The advantages of this method are (1) Excellent hemostasis, (2) skin crypt sterilization is accomplished, (3) no absorbable suture material is left buried in the wound, (4) drainage is unnecessary. Its disadvantages are (1) Cannot be employed in the presence of ether or other inflammable general anesthetic agents, (2) slight tendency for aseptic skin slough at lower angle of wound.

CONCLUSION

The use of electrosurgery as an aid in the operative treatment of hydrocele is apparently of value and is worthy of further trial.

UNILATERAL AGENESIS OF THE MÜLLERIAN SYSTEM IN THE FEMALE

CASE REPORT

LEONID S CHERNEY, M D

SAN FRANCISCO, CALIF

FROM THE DEPARTMENTS OF SURGERY AND ANATOMY UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL
SAN FRANCISCO, CALIF

Embryologic Considerations—The müllerian ducts first appear in the embryo during the sixth week of development, at the anterior ends of the wolffian ridges, on their ventrolateral aspects. The solid process of cells forming each müllerian duct reaches the cloaca after a week's growth, and subsequently develops a lumen. In the male fetus, atrophy of the müllerian ducts begins in the third month, but in the female development continues. The cephalic portions of the müllerian ducts form the uterine tubes, while the caudal portions fuse, giving rise to the uterus and, later, to the vagina. The fused medial walls of the two ducts degenerate, thereby creating a single-barreled uterus and vagina. The ligamentum teres (the homologue of the gubernaculum testis in the male) arises as a condensation of mesenchyme in the inguinal fold of

peritoneum, although attached to the mullerian duct, its origin is independent of that structure

The type of malformation of the uterus, the vagina and the tubes depends on the embryonic age at which the development of the mullerian system deviates from the normal or becomes arrested. During the first month there may be unilateral or bilateral failure of development. During the second month, the two sides may fail to fuse, with the result that a double uterus and vagina are

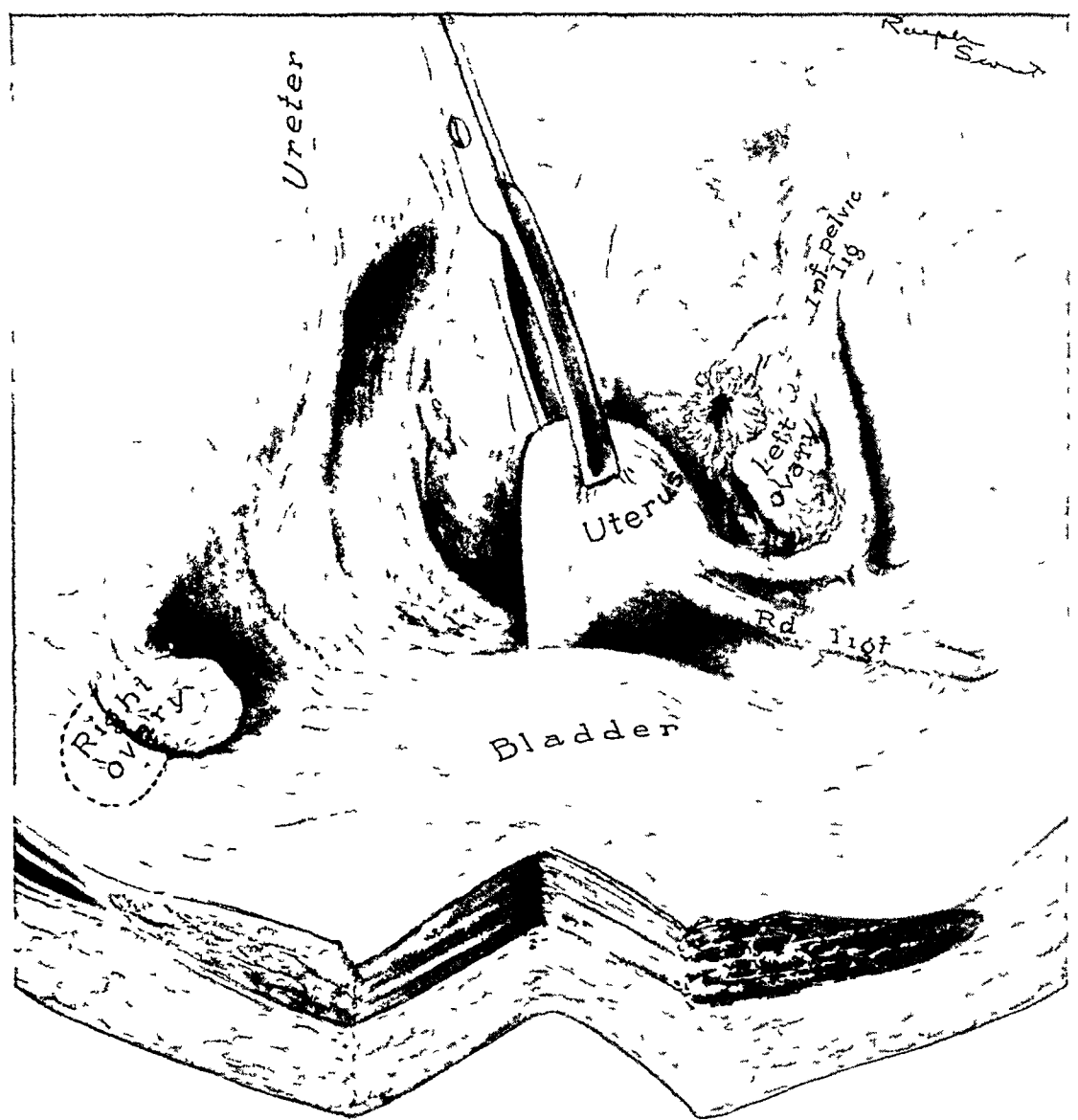


FIG. 1.—View of the pelvic viscera. Note the congenital emptiness of the right side of the pelvis

formed (uterus didelphys), or the arrested development may be unilateral, resulting in a rudimentary horn on one side. In the third and fourth months there may be incomplete fusion of the two mullerian ducts, giving rise to a uterus with two distinct horns (uterus bicornis), or a uterus with a concave fundus (acuate uterus), in either form the septum may or may not persist and the cervix may be single or double. After the fifth month, the only anomaly is an acuate uterus. In addition to the anomalies mentioned above, there may

the persistence of the septum in a uterus which appears externally normal. This septum may or may not extend into the vagina (uterus septus duplex or uterus et vagina septus duplex).

The type of anomaly presented in the appended case report is exceedingly rare. The only reference to it found in the literature is in Fritz Kermauner's chapter on the malformations of the female genital apparatus in Halban's System of Gynecology. He states that although there are infrequent case reports of hemiuterus, on close scrutiny they turn out to be uteri with a rudimentary horn. In an exhaustive survey of the literature of the preceding 100 years, Kermauner quotes only three instances where he was reasonably certain that there was a complete unilateral agenesis of the müllerian duct.

Case Report—The patient was an unmarried, white female, age 32, who complained of periodic attacks of pain in the right lower quadrant of the abdomen. They had first appeared in May, 1935, slowly increased in severity and had become intense four weeks before her first visit, in May, 1937. There had been a loss of five pounds in weight. The pain was cramp-like in character, and occasionally was accompanied by nausea, but never by vomiting, it was most pronounced during the four days preceding each menstrual period and was aggravated by putting the abdominal wall under tension. It was not affected by diet, meals or stools, relief was obtained by lying down with the thighs flexed.

Her menses had always been regular, every 28 days, lasting from three to six days, with a moderate flow, prior to the onset of the present illness they had not been accompanied by pain. There was no history of any specific infection and her past history was entirely negative.

Physical Examination was not remarkable except for the abdominal and the pelvic findings. There was deep tenderness at McBurney's point. The vagina admitted two fingers. The cervix was pointing to the right and there was a slightly tender mass, vague in outline, in the left fornix.

Operation—Upon opening the abdomen it was noted that the uterus was small and tilted to the left, with the right and superior surfaces meeting at right angles, it was obviously a left hemiuterus. The left broad ligament with its contents was normal in appearance. On the right, the broad ligament, the tube, and the abdominal portion of the round ligament were completely absent, leaving the right half of the pelvic cavity empty. The right ovary, normal in size and appearance, was situated at the internal inguinal ring, partly drawn into the inguinal canal by the ligamentum teres to which it was attached (Fig. 1).

The ovary was disengaged from the inguinal ring and, to prevent the recurrence of herniation, the round ligament was sutured to the deep aspect of the aponeurosis of the external oblique muscle, as in a modified Gilliam suspension of the uterus.

The patient had an uneventful convalescence. She has been completely relieved of her symptoms and has regained her normal weight.

ANNOUNCEMENT OF THIRD INTERNATIONAL CANCER CONGRESS

THE THIRD INTERNATIONAL CANCER CONGRESS under the auspices of the International Union Against Cancer, whose headquarters are in Paris, will be held at the Chalfonte-Haddon Hall, Atlantic City, New Jersey, September 11-16, 1939

The President of the Congress is Dr. Francis Carter Wood, Director of the Institute of Cancer Research of Columbia University. The executive officers are physicians well known for their experience in these matters. Dr. Donald S. Childs, of Syracuse, is Secretary-Treasurer, Dr. Eldwin R. Witwer, of Detroit, is in charge of the scientific exhibits, and Dr. A. L. Loomis Bell, of Brooklyn, is handling the commercial exhibits and transportation.

The Congress has been divided into Groups under Section Chairmen, of whom Dr. John D. Camp, of the Mayo Clinic, will handle Diagnostic Roentgenology, Dr. Uisus V. Portmann, of the Cleveland Clinic, Radiotherapy, Dr. Frank H. Lahey, of the Lahey Clinic, Boston, Surgery, and Dr. C. C. Little, of the Jackson Memorial Laboratory, Bar Harbor, Maine, Genetics. The program on Experimental Pathology has been organized by Dr. William H. Woglom, of the Institute of Cancer Research of Columbia University, General Pathology is under that able teacher, Dr. Milton C. Winternitz, of Yale University, Radiobiology and Radiophysics have for Chairman Dr. G. Failla, of the Memorial Hospital, New York, and Dr. Burton T. Simpson, of the State Institute for the Study of Malignant Disease, Buffalo, is Chairman of the Section on Statistics and Education. Numerous assistant chairmen have been appointed.

A number of sections will include elaborate symposia on special topics. For example, there will be a combination meeting to discuss the treatment of the lymph nodes of the neck after the destruction of the primary neoplasm. A number of similar combination meetings will be held.

A rather unusual feature of the Congress is that the evenings will be devoted to addresses by well-known experts. For instance, on Monday evening, Dr. A. Lacassagne, of the Radium Institute of Paris, will give a survey of the relation of estrogens to malignancy, and Dr. C. C. Little, of Bar Harbor, Maine, will summarize our knowledge concerning genetics and tumors. On Tuesday evening, Drs. J. W. Cook and E. L. Kennaway, of London, will discuss the "Chemical Compounds as Carcinogenic Agents," and Dr. W. E. Gye, also of London, will report on the viruses. On Wednesday evening, it is expected that Senateur Justin Godart, former Minister of Health in France and President of the International Union Against Cancer, will make a short address, followed by Surgeon General Thomas Parran, of the United States Public Health Service, who will discuss phases of the Government activity in the investigation and treatment of cancer. Thursday

evening will be devoted to talks on the developments in surgery by Dr Frank H Lahey of Boston, and the organization of a Cancer Clinic by Professor Fred J Hodges of Ann Arbor, Michigan. Friday evening, the Congress will be closed by an address from Dr S Bayne-Jones, Dean of the Yale University School of Medicine, and by Professor James Ewing, of the Memorial Hospital, New York, who will summarize what has been accomplished and what should be done for the cancer problem in the future.

Extensive commercial and scientific exhibits have been arranged. Projection apparatus of all types will be available, and judging from the number of papers already received the Congress will be an outstanding one. Official delegates will be present from various foreign countries, including England, France, Belgium, Germany, Switzerland, Poland, Hungary, Italy, Russia, Chile, Argentina and other countries in South America.

BOOKS RECEIVED

THE receipt of books for review is hereby acknowledged. This statement shall be regarded as sufficient acknowledgment of the courtesy of the publishers. Selections will be made for review predicated upon the interests of the readers of the ANNALS OF SURGERY and as space permits.

MODERN SURGICAL TECHNIC. By Max Thorek, M D. Philadelphia: J B Lippincott Co., 1938.

SURGICAL TECHNIQUE AND PRINCIPLES OF OPERATIVE SURGERY. By A V Partipilo, M D. 3rd Ed. Chicago: The John Maher Co., 1938.

SPINAL ANESTHESIA. By Louis H Maxson, M D. Philadelphia: J B Lippincott Co., 1938.

HANDBOOK ON CANCER. By Cancer Control Commission, Canadian Medical Association, Toronto, Canada. Murray Co., Ltd., 1938.

THE 1938 YEAR BOOK ON GENERAL SURGERY, Edited by Evarts A Graham, M D. GENERAL MEDICINE, Edited by George F Dick, M D, J Burns Amberson, Jr, M D, George R Minot, M D, S D, F R C P (Hon.) Edin., William B Castle, M D, M D (Hon.) Utrecht, William B Stroud, M D, and George B Eusterman, M D. EYE, EAR, NOSE AND THROAT, Edited by E V L Brown, M D, Louis Bothman, M D, Samuel J Crowe, M D, and Elmer W Hagens, M D. The Year Book Publishers, Inc., Chicago, 1938.

TEXTBOOK OF NEURO-ANATOMY AND THE SENSE ORGANS. By O Larsell, Ph D, New York and London: D Appleton-Century Co., Inc., 1939.

ANATOMY OF THE HUMAN LYMPHATIC SYSTEM. By H Rouviere, Professor of Anatomy at the Medical Faculty of Paris, France. Translated by M J Tobias, M D. Edwards Bios, Inc., Ann Arbor, Michigan, 1938.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY.

Walter Estell Lee, M D

1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T Pilcher, M D, Managing Editor, 121 Gates Avenue, Brooklyn, N Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa



SURGICAL MANAGEMENT OF THE PATENT DUCTUS ARTERIOSUS*

WITH SUMMARY OF FOUR SURGICALLY TREATED CASES

ROBERT E. GROSS, M.D.

BOSTON, MASS

FROM THE CHILDREN'S HOSPITAL, THE PETER BENT BRIGHAM HOSPITAL, AND THE SURGICAL LABORATORY OF THE HARVARD MEDICAL SCHOOL, BOSTON, MASS

DURING FETAL LIFE the incomplete expansion of the lungs produces a high resistance to blood flow in the pulmonary vascular bed. It is necessary, therefore, to have a compensatory mechanism whereby blood can be short-circuited around the lungs. Nature provides this shunt in the form of the ductus arteriosus which diverts blood from the pulmonary artery directly into the aorta. When the fetus is born and the lungs expand, the ductus normally closes and all of the blood passes through the lung bed to be aerated. If this vessel fails to close, a reversal of flow takes place within the ductus because pulmonary artery pressure is reduced and aortic pressure is increased. Blood then passes from the aortic arch into the lesser circulation (Fig 1) and the patient possesses what is essentially an arteriovenous aneurysm (Holman¹⁴).

There is considerable difference of opinion regarding the time when the ductus Botalli ceases to function. Patten²⁰ has pointed out that degenerative intimal changes begin in the latter part of fetal life, and it is his concept that increasing amounts of blood flow through the lungs even before birth. The histologic findings in the closing ductus resemble those of endarteritis obliterans, according to Schaeffer's²⁴ studies, and the diminution in size of the vessel is a gradual process requiring many weeks before occlusion is completed (Scammon and Norris²³). Christie⁵ studied a large series of routine postmortem specimens from babies to determine the time at which the ductus was normally obliterated. As older and older subjects were examined, the number of open ducti diminished to 44 per cent at one month, 12 per cent at two months, and 2 per cent at eight months of age (Chart 1). Following this, there was a small group of individuals in whom the vessel remained open permanently. At what age, then, can the persistence of the vessel be considered as pathologic? Arbitrarily, we might say that the ductus Botalli which is still open after the first year of life should be regarded as abnormal.

The child or youth who possesses a patent ductus faces an uncertain future. He may live in relatively good health till old age, or his life might be quickly terminated by some complication arising from his long existing lesion. Like

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

Damocles, he leads a precarious existence, never knowing when he might be cut down by the danger which menaces him. The causes of death in these individuals may be listed as rupture of the ductus, thrombosis of the ductus with subsequent embolism, bacterial endocarditis or endarteritis, and cardiac decompensation resulting from the arteriovenous communication.

In 1907, Munio¹⁹ first suggested that the surgeon might undertake the task of obliterating the ductus by operative means. So far as I am aware, O'Shaughnessy²² and Strieder⁹ have been the only ones to attempt perform-

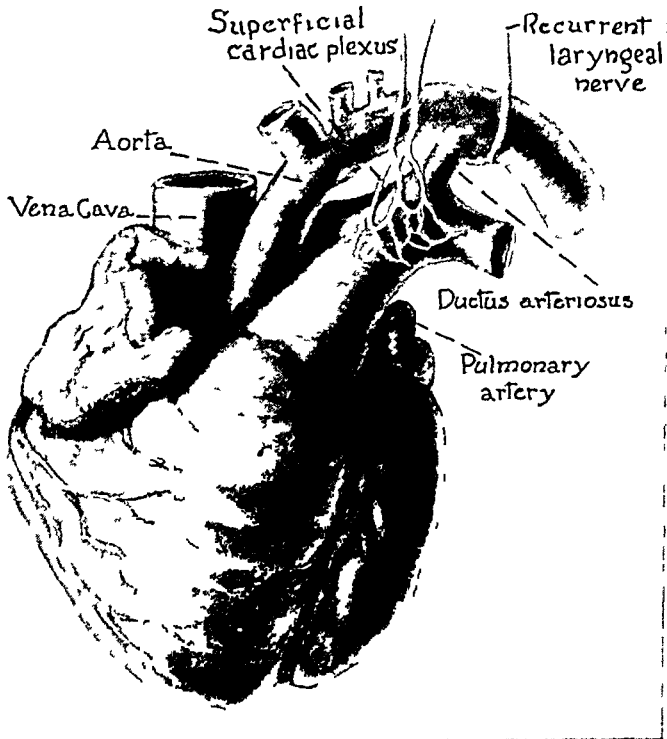


FIG 1.—Drawing of heart and great vessels from a four weeks old child showing position of the ductus arteriosus and its communications with the pulmonary artery and aorta. The left recurrent laryngeal nerve curves around the aortic arch lateral and posterior to the ductus. The superficial cardiac plexus which lies between the arch and pulmonary artery is joined by small nerves from the vagus and cervical sympathetics which lie in front of the arch and medial to the ductus.

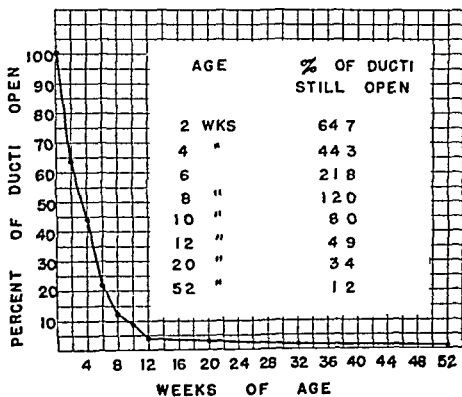


CHART 1.—Showing time of closure of the ductus arteriosus as found by examination of routine autopsy material (From Christie 5)

ance of this feat. In O'Shaughnessy's patient, the diagnosis was incorrect and the ductus was found obliterated. In Strieder's case, technical difficulties prevented complete closure of the vessel and the patient succumbed a few days later. My attention was first directed to the problem several years ago by Dr. Elliott Cutler, but the present work had its greatest impetus from the enthusiastic support of Dr. John Hubbard who presented Case 1 for study and subsequent operation. The cases herein reported are the first and only ones which have ever been

successfully operated upon. There is much to be learned concerning the best method of obliterating the ductus, but the work here presented amply demonstrates that the ductus can be explored with safety and that it can be ligated in most instances without mortality. The degree of success thus far encountered makes it important to recognize these patients—and not merely classify and treat them as “congenital heart disease”—because in properly selected cases surgical therapy has much to offer.

Etiology of the Persistent Ductus Arteriosus—The embryonic shunt between the pulmonary artery and the aortic arch may persist into postnatal life as a compensatory mechanism. Thus, if there is obstruction at the aortic valve from bicuspid or stenotic leaflets, or if there is coarctation of the aortic arch, the ductus may remain open and allow blood to escape from the pulmonary artery to the aorta. Such a combination is rare, and when it does occur it is necessarily accompanied by some degree of cyanosis. A second compensatory mechanism is concerned with stenosis or atresia of the pulmonary valve or hypoplasia of the pulmonary artery, wherein the direction of blood flow through the ductus must be from aorta to pulmonary artery. In this latter type of case there are usually other associated anomalies, the most frequently encountered combination being the tetralogy of Fallot in which there are stenosis of the pulmonary valve, a defect of the interventricular septum, hypertrophy of the right ventricle, and a right-sided aorta.

While it is true that the open ductus may often represent a compensatory mechanism, it may also exist without any other abnormality. In a series of 242 cases reviewed and studied by Abbott,¹ there were 92 hearts in which there were no other cardiovascular lesions. In short, about two-thirds of patients with a patent ductus have some other abnormality and about one-third of them have no other pathologic finding.

In those cases in which the open ductus is the sole lesion, there is no adequate explanation for the continued patency of the vessel. There are, however, three things which must be considered as possible etiologic factors. The first of these is concerned with the anatomic position and direction of the vessel. If one examines postmortem material of infants who have died in the first few months of life, the ductus, or its obliterated remnant, sweeps backward and to the left with a gradual curve to run alongside the aorta and then to enter it at a rather acute angle. The nature of this angle of entrance into the aortic arch in the fetus obviously has the function of directing the oxygen-deficient blood from the right ventricle downward in the aorta so that it might be distributed to the hypogastric arteries and thence to the placental circulation. The sharpness of this angle must serve another purpose, namely, to help obliterate the ductus in postnatal life. At birth, when the lungs expand and the blood flow through them increases, a diminishing amount of blood is forced from the pulmonary artery into the ductus. When this state of affairs obtains, the arterial blood rushing around and down the aortic arch must now have somewhat of a sucking action on the ductus which enters it so acutely. This sucking action would tend to collapse the vessel.

If, however, the ductus joins the arch at a more obtuse angle or at a right angle, the lumen of the ductus will be subjected directly to the high pressure existing in the aortic arch, and the ductus will thereby be kept distended. Thus, it is probably correct to believe that the principal reason for persistence of a ductus is due to its anomalous position and direction. This idea is certainly sustained by the observations in all four of the cases here reported.

A second possible factor which might contribute to the persistency of a ductus is some defect in its wall. This deficiency may concern the internal elastic membrane, the elastic tissue of the media, or even the smooth musculature. Such deficiencies of the ductal wall would allow the vessel to distend under low internal luminal pressures which would not distend a vessel possessing normal elasticity. Such a consideration is hypothetical, for there is no published account of histologic examination of the wall of persistent ductus compared with those which are normally closing in the first or second month of infancy. It is certainly true that a thin, inelastic wall is not seen in all cases of persistent ductus, but in one patient (Case 2) the vessel wall was as thin as a vein. That a thin or deficient wall might be a factor in persistency in some instances is also supported by those cases in which the ductus has actually dilated to aneurysmal proportions.

The third factor concerned with the persistency of the ductus is related to its neuromuscular control. The smooth muscle fibers in the ductal wall of some animals have been shown to be under vagus nerve control. Barclay, Barcroft, Barron, and Franklin² have injected radiopaque substances into the vascular systems of lambs delivered by cesarean section and have observed the ductus roentgenologically. It was their belief that the ductus underwent a "functional closure" within a few minutes after birth. However, subsequent autopsy upon such an animal showed the ductus to be still morphologically open. The only way to correlate these findings was to assume that the ductus was *functionally* closed during life by a neuromuscular mechanism which, of course, would not be operative after death. It is not reasonable to assume that the ductus is held in a state of obliteration throughout the newborn period by smooth muscle contraction alone. However, it is probably true that contractions assist in the closure of a ductus and that a deficiency in the neuromuscular apparatus would tend to make morphologic obliteration more difficult.

Pathologic Anatomy—The length and diameter of the ductus, as well as the thickness of its wall, have considerable bearing on the possibilities of surgically ligating it. Unfortunately, the literature gives but scanty account of desired anatomic facts. In most instances the internal diameter of the lumen is about all that is listed. The following descriptions are gleaned from diverse sources and represent statements from various authors, postmortem observations we have made ourselves, and further findings observed in four operative cases.

The size of the ductus cross-section is variable. An internal diameter of 3 to 4 Mm. is not uncommon, but in many cases this may be as much as 6

to 8 Mm or more. In one autopsy specimen I have seen, from a man dying at 17 years of age, the ductus was 7 Mm in diameter in its postmortem state, and, of course, may have been larger when distended during life. In the four cases operated upon, the external diameters of the ducti were 8, 12, 7 and 8 Mm in individuals who were seven, 11, seven, and 17 years old, respectively. In general, it has been my experience that the ductus was about the same size as the left subclavian artery as it left the aortic arch, but in Case 2 it was considerably larger than this vessel.

The length of the ductus is of great importance, for, if the vessel is very short, dissection between the aortic arch and pulmonary artery may be impossible. In some adults¹⁵ the ductus is so short that a direct communication exists between pulmonary artery and aorta—an anatomic arrangement which would make it practically impossible to close the shunt. In newly born infants the ductus is usually 1 to 1.5 cm long. In the four operative cases neither of these extremes was found, the length of these vessels being 5, 12, 7 and 5 Mm respectively. In each of these cases, the first appearance at operative exposure suggested that there was a direct opening from aorta to pulmonary artery, but on careful and slow dissection of fatty and areolar tissue the aorta and pulmonary artery could be separated so as to bring into view a ductus which was long enough to ligate.

The thickness of the ductal wall varies. It is gathered from autopsy descriptions that the vessel is usually about as thick as an artery of similar size. In Cases 1, 3 and 4 this appeared to be so, but making this assumption in Case 2 nearly led to a fatality. In this latter operation, dissection was begun believing that the ductal wall would stand considerable manipulation, only to find that it suddenly tore and copious hemorrhage ensued. The torn wall was then seen to have the consistency and thickness of a vein. This possibility must be remembered when handling the vessel during life.

The swirling and impinging of blood currents against the pulmonary artery wall over a period of years eventually leads to intimal thickening, cholesterol deposition, and formation of typical atheromatous plaques. These changes are primarily found around the pulmonic orifice of the ductus and also on the wall opposite to the opening of the ductus. It is at these sites of intimal damage that subsequent bacterial endarteritis is apt to begin. Matusoff¹⁶ and Schlaepfer²⁵ have summarized the postmortem findings in cases of patent ductus arteriosus with infective pulmonary endarteritis.

Prognosis—It is largely conjecture to estimate the prognosis for a given individual. Statistics taken from the literature give a false idea of the life expectancy, due to the fact that patients dying of some other cause are apt to go unrecorded, whereas individuals dying from complications of a patent ductus are more likely to be reported. Therefore, a summary of the literature gives a more serious outlook than the lesion probably warrants.

Cardiologists, with any breadth of experience, have examined and cared for adults who have patent ducti and yet lead rather normal lives. There is a general feeling that more of these cases are seen in childhood or adolescence.

than are encountered in the latter half of life. One of two things must happen. Either these people grow up and die of their lesion after having been lost sight of, or else they have spontaneous closure of the ductus during middle life. Which of these interpretations is correct is difficult to say, but the net result is that many clinicians have developed the belief that the patent ductus carries a fairly good prognosis.

Opposed to this preceding, rather optimistic view, one finds a darker side when reviewing the literature on the subject. Numerous case reports are encountered describing patients who were known to have a patent ductus without apparent disability throughout adolescence, but who then died of decompensation or subacute bacterial endocarditis^{15, 21, 27}. There is no apparent method of computing the prognosis because the number of people with patent ductus is too small for adequate study. In all probability, the truth lies somewhere between the optimistic and the pessimistic point of view.

Abbott¹ has listed 92 patients with autopsy proof of a persistent ductus without other demonstrable cardiovascular anomaly. Twenty-eight of these died of subacute bacterial endocarditis, 24 died of slow cardiac decompensation, and 16 died of rather sudden cardiac failure. Two died of rupture of the ductus. The remainder died of causes unrelated to the circulatory system. In this series, then, the incidence of death from endarteritis or endocarditis was 30 per cent and the incidence of cardiac decompensation was 43 per cent. The average age of death was 24 years.

The complications attendant to the presence of a patent ductus may be summarized as fourfold. First, the existing shunt diverts sufficient blood from the aortic circuit so that the peripheral blood flow is deficient, and the growing child is thereby deprived of proper nutrition. Second, in rare cases a thinned-out ductal wall may dilate⁶ and rupture¹⁷. Third, the presence of this vascular abnormality carries with it a high danger of subacute endocardial infection from the *Streptococcus viridans* or acute vegetative endocarditis from other organisms. Fourth, the shunt from the aorta to the pulmonary artery places a great burden on the heart by enormously increasing the total amount of blood which the left ventricle must put out per minute and by increasing the resistance against which the right ventricle must pump blood. The cardiac reserve is thereby reduced and myocardial failure may supervene after one or two decades.

Clinical Signs and Symptoms—About two-thirds of the patients are females. A retardation in physical development is extremely common. Mental development, however, is usually good. The clinical course with an uncomplicated patent ductus may show little variation from the normal or there may be findings of a profound cardiovascular abnormality¹⁸. The general run of cases develop but slight cardiac embarrassment in the early years of life. Physical activity is only slightly limited throughout childhood and adolescence, but these youngsters often notice that they tire more easily and become more dyspneic than confreres of their own age or size. Epistaxis may be profuse, particularly in children four to eight years of age. These patients

are usually conscious of a greatly intensified heart beat which is particularly exaggerated by exercise. A "buzz" or "burr" or "hum" in the chest is frequently spontaneously noticed by the individual. At times the mother will volunteer the information that she feels a "buzz" (as she calls the thrill) when dressing, bathing, or otherwise attending her child.

In contrast to this above described rather mild and attenuated course, occasional patients give symptoms of early cardiac embarrassment as is typified in Case 4. This girl experienced little difficulty until the fifth or sixth year of life when there was marked cardiac disability for which she was institutionalized for half a year. She then regained compensation and progressed fairly well until high school age. With the increased activity demanded by this stage of schooling, periods of semi-invalidism occurred during which she had edema of the legs, cough, some orthopnea, and occasional nocturnal dyspnea leading to a restricted or bedridden existence for two or three months at a time.

The physical manifestations of a patent ductus may be entirely wanting in infancy, are apt to be confusing in the first two or three years of life, but are almost always typical after the fourth year. In the first year there may be no murmur, thrill, or cardiac enlargement. In the second and third years some cases show only mild cardiac enlargement and a systolic murmur which is loudest at the base. At this stage one is usually not justified in making a more accurate diagnosis than "congenital heart disease." By the third or fourth year the murmur becomes continuous, develops a "machinery" character, is accentuated during systole, is loudest in the pulmonic area, and becomes accompanied by a systolic or continuous thrill. This progression of signs takes place with varying rapidity, requiring a year in some cases or several years in other individuals.

By the fourth or fifth year the fully developed picture of a patent ductus is present and may be described as follows. The heart action is extremely forceful and overactive and the rate may be increased. There is a loud, rough, continuous murmur with systolic accentuation, heard best in the second or third interspace to the left of the sternum. The quality of this murmur has been described as sounding like "machinery," "train in a tunnel," "mill wheel" or "rumbling thunder." The murmur is transmitted widely over the precordium with only slight diminution, but its quality may be somewhat changed toward the apex. The entire murmur, or only its systolic element, is transmitted to the back, to both axillae—particularly the left—with rather loud intensity, but it is heard only faintly in the neck. There is almost always a precordial thrill which is either systolic or continuous and which is most intense in the pulmonic region. The second sound at the pulmonic area is greatly increased and has a snapping quality. Cardiac enlargement may possibly be made out by percussion. The systolic blood pressure is within the normal range. Bohn³ pointed out that the diastolic level is low (when the ductus is large enough) so that these individuals have a high pulse pressure similar to that seen in regurgitation at the aortic valve. With this high pulse

pressure there is a collapsing type of pulse, possibly a "pistol shot" sound over the large leg and arm arteries, and a visible capillary pulsation in the skin or nail beds. One of the interesting features about the low diastolic pressure is the fact that it becomes lower still during exercise (in contrast to the normal rise during physical exertion).

In rare cases there may be changes in the voice. Schlotter²⁶ described one patient in whom laryngeal examination showed the left vocal cord completely immovable, but no abnormality was made out on the right. The voice was clear. A huge ductus was pressing on the left recurrent laryngeal nerve.

Roentgenologic and Laboratory Findings—Roentgenologic examination of the heart is usually not necessary to make the correct diagnosis, but it does offer confirmatory evidence in most cases. Wessler and Bass²⁸ early emphasized the importance of roentgenography as a diagnostic aid. In the first year or two of life the picture may be distinctly confusing and contribute little. During this period there may be nothing more than slight cardiac enlargement with a rather globular shape to the organ in the anteroposterior view. After the third or fourth year, however, the roentgenologic findings are apt to be typical in the uncomplicated case. There is mild or moderate cardiac enlargement, particularly of the left ventricle. The pulmonary artery (often incorrectly called the pulmonary "conus") is more prominent than normal, though there are recorded instances in which this was not found. In all four of our patients this vessel was regarded as protruding unduly toward the left (Figs 4, 9, 11 and 16). The lung fields have increased markings due to the vascular congestion in the lesser circulation. Fluoroscopically, the heart shows a very forceful action and there is increased pulsation in the dilated pulmonary artery. The increased pressure in the smaller pulmonary arteries throughout the lung fields may impart to them a pulsation which is seen as a "hilar dance." This, however, may be quite hard to detect.

In two of our patients there has been an interesting finding in regard to the size of the left auricle. In Case 3, this chamber was distinctly enlarged in the right oblique view. This posterior enlargement of the left auricle in a young child was at first believed to be due to an associated interauricular septal defect. We are now forced to believe that this thin-walled chamber can dilate in the presence of a patent ductus because of the enormous amount of additional blood which enters the pulmonary circuit from the aorta, and which must circulate through the left auricle. The correctness of this tenet was strikingly substantiated by the findings in Case 4, in which the dilatation of the left auricle led to the belief that an associated mitral stenosis was present. Here again there was a striking diminution in size of the left auricle after surgical obliteration of the ductus. (The cause for this dilatation may be appreciated by the fact that blood flow studies on Case 4 showed that 5.8 liters of blood per minute were passing through the right auricle and ventricle—an essentially normal figure—but concurrently, 24.6 liters were flowing through the left auricle and ventricle. Under these circumstances there is

some dilatation of the thick-walled left ventricle and a marked dilatation of the thin left auricle)

In one case we attempted to outline the interior of the cardiac chambers by injection of radiopaque media into an arm vein. While the studies in this case were not entirely satisfactory, the observations were of value in that no other intracardiac pathology was demonstrated. This examination is useful in order to rule out other associated lesions such as septal defect, pulmonary stenosis, or hypoplasia of the aortic arch.

The electrocardiographic tracings are reported as demonstrating left axis deviation when the work of the left ventricle is great, or right axis deviation when the right auricle must pump blood against an increased pulmonic artery pressure. While both of these findings are possible, none of our cases showed axis deviation (Graph I), and we have come to look upon an abnormal electrocardiogram as possibly indicating some other associated malformation. While the EKG is of little aid in making the diagnosis, it is of some use in ruling out the presence of other abnormalities such as pulmonic stenosis or atresia.

Compensatory polycythemia does not occur to any important degree and it is rare for the erythrocyte count to be over five or five and one-half million. Blood volume studies have not been extensively performed, but the available data indicate that there is moderate increase in the cellular and plasma elements of the blood. In Case 4 the blood volume was 3,950 cc. as compared to an expected normal of 3,200 cc. for this age and size. The circulation time from arm vein to tongue is normal or prolonged.

Criteria in Selection of Cases for Operation—In reviewing a number of cases from the Cardiac Clinics of the Children's Hospital and the Peter Bent Brigham Hospital, we have formulated certain criteria for the selection of cases in which operative intervention is to be proposed. An increased experience will probably alter our views somewhat, but for the present the following considerations must be made in evaluating a given case for possible surgical therapy.

Providing the diagnosis of patent ductus is reasonably established, it is essential to rule out other associated conditions, the nature of which would make it dangerous to close the ductus. Such lesions would be stenosis of the aortic valve, hypoplasia or coarctation of the aortic arch, stenosis or atresia of the pulmonary valve, and bacterial endocarditis. Any one of these is a definite contraindication to operation. Systolic or diastolic murmurs over the aortic area which do not appear to be transmitted from the pulmonic area are highly suggestive of aortic stenosis or insufficiency, particularly if accompanied by a left axis deviation in the electrocardiogram. Hypoplasia of the aortic arch can be excluded by proper fluoroscopic examination. Coarctation will show a lower blood pressure in the legs than in the arms, the reverse of normal. Stenosis of the pulmonic valve may be exceedingly difficult to diagnose because the murmurs arising from it are almost identical with those originating from the ductus. However, the patient with an uncomplicated patent ductus has

a loud snapping second pulmonic sound due to the increased pressure within the pulmonary artery, whereas the pulmonic second sound will be absent or diminished if there is an abnormality of the valve. Furthermore, pulmonic stenosis is practically always accompanied by some right-sided hypertrophy in the roentgenogram, by right axis deviation in the electrocardiogram, and by cyanosis due to a right-left shunt of blood through a septal defect. Subacute bacterial endocarditis must be regarded as a contraindication to operation because the friable vegetations around the ductal opening will almost certainly be dislodged and result in embolism or a more severe bacteriemia.

There are several lesions, the presence of which do not necessarily imply that operation should be abandoned. The postoperative results following ligation of a ductus, when there is an associated septal opening or a mild mitral (rheumatic) stenosis, will not be as satisfactory as those obtained when the ductus is the sole lesion. However, a heart which is laboring because of two defects can be improved if one of these is removed. For this reason, we do not regard a septal defect as a contraindication to operation. Likewise, in Case 4 the possibility of a superimposed rheumatic mitral stenosis was raised, but closure of the ductus was recommended.

Confining ourselves now to those cases with a patent ductus and no other demonstrable cardiovascular lesion, the question arises whether all such individuals should be operated upon. The answer is decidedly, "No!" There are without doubt some individuals who have a patency of the ductus in infancy or early childhood and who have later findings indicating that this arterial shunt is spontaneously closing itself. Hence this individual should be left alone and natural processes permitted to continue in the reduction of size or ultimate obliteration of the vessel. When such a person is followed over a period of years, the murmurs have a decreasing intensity, lose their harshness, and may disappear from the diastolic phase of the cardiac cycle. The thrill, likewise, diminishes in intensity and may change from a continuous one to a systolic type. The heart is not enlarged, even though there may be a fulness of the pulmonary artery. The heart is able to maintain adequate peripheral circulation as is indicated by a normal diastolic pressure. In such children we feel that dangers of operation are not warranted when the ductal size is either stationary or is diminishing. In contrast to this, there are other patients in whom the clinical signs point to the fact that the ductus is actually becoming larger or that there are early signs of cardiac embarrassment. When once this trend of affairs is recognized it is reasonable and desirable to propose operation.

The positive criteria for selection of cases for operation may then be enumerated as follows: (1) There must be reasonable assurance that the ductus is patent as is determined by a loud, continuous, machinery murmur in the pulmonic area accompanied by an increased second pulmonic sound and a systolic or continuous thrill which is most intense in the pulmonic region. (2) There should be evidence of congestion in the lung fields by roentgenologic examination. (3) There should be a prominence of the pul-

monary artery roentgenologically—though some cases have been reported in which this has been absent (4) There should be roentgenologic evidence of cardiac enlargement, particularly in the region of the left ventricle (5) There should be a peripheral blood pressure which has an essentially normal systolic level, but a definitely lowered diastolic level In short, one should have an indication that the ductus is enlarging, that the individual is not developing properly, that the danger of bacterial endarteritis is high, or that the heart is carrying an increased burden

The Operative Exposure and Obliteration of the Ductus Arteriosus—The ductus can be exposed by an anterior, transmediastinal route, opening through the sternum and viewing the great vessels very much as one does for pulmonary embolectomy There is little to recommend this approach, for the opening in the chest wall is relatively small and the operator would be working in the bottom of a deep, narrow hole With such limited exposure it would be exceedingly difficult to carry out any adequate dissection between the aorta and pulmonary artery and to control any bleeding which might be encountered Furthermore, there would be great danger of injuring the superficial cardiac plexus and the left recurrent laryngeal nerve In favor of the transmediastinal approach is the fact that the lungs are not collapsed, but in view of general experience with the innocuousness of temporary collapse this advantage cannot be regarded as important

At the beginning of the present work it was necessary to devise a method by which the ductus region could be exposed adequately, safely, and without great shock After examining a number of human cadavers, it was apparent that the aortic arch and pulmonary artery could be approached better from the left side than from the front of the chest Making use of these observations, experimentation was then performed on living dogs, and it was found that an admirable view of the ductus was obtained by entering the thorax through the left pleural cavity and temporarily collapsing the lung during the operation This operative approach has been treated more fully in another publication (Gross¹⁰) and, as it applies to the human, it may be described as follows

The patient is placed on his back, with the left arm extended up along the head and with a small sandbag beneath the left shoulder so as to elevate the upper portion of the left side of the chest A transverse incision, slightly concave toward the patient's head, is made either just above or below the breast tissue, from the sternal margin to the anterior axillary line This is carried down through the subcutaneous tissues, the pectoralis fascia, and the fibers of pectoral major and minor muscles (While this incision has been employed in all the cases here reported, a lower incision which turns upward the entire breast and pectoral muscle group would be an acceptable procedure but would not produce quite so good an exposure) The pleural cavity is entered through the third interspace, carrying the incision from the internal mammary vessels around to the midaxillary line The internal mammary vessels need not be divided The third costal cartilage is cut across and, if it

is desired, the second cartilage may also be divided (In one patient a better opening was made by entering through the second interspace and retracting the second rib upward) This allows the ribs to separate easily with the aid of a self-retaining retractor. As the lung collapses away inferiorly it is protected by a covering of moist gauze.

With the lung out of the way, the operator now has an excellent view of the lateral aspect of the base of the heart and the superior mediastinum (Figs 10 and 12). The phrenic nerve is readily seen beneath the thin pleura but the vagus nerve may or may not be clearly discernible, depending upon how much fibro-fatty tissue there is around it. Superiorly, the rounded arch of the aorta is easily identified, and if all the major vessels arising from it cannot be seen, at least the first portion of the left subclavian artery can be viewed. The pleural covering of the mediastinum is now incised from the lung root upward toward the base of the neck to uncover the pulmonary artery and aortic arch. This incision is 7 or 8 cm in length and should be made 1 to 2 cm posterior to and parallel to the phrenic nerve. This incision is placed well behind the phrenic nerve in order to avoid injury to the underlying superficial cardiac plexus and the fibers which join it from the sympathetic and vagus systems (Fig 1). In some individuals the upper one or two left intercostal veins do not drain into the azygos system, but instead form a single trunk which courses medially forward and along the mediastinal surface to flow upward to the left innominate vein. Inasmuch as this vein crosses the cephalic end of the desired pleural incision, it is best to divide it when present.

After the pleura is incised, a fine network of fat and areolar tissue of variable vascularity is found filling in the sulcus between the aortic arch and pulmonary artery. Almost invariably, it first appears that these two great vessels are directly contiguous to one another and that any communication between them must be in the form of a direct opening. However, with great care and patience, it is surprising to find that a plane of cleavage can be located and if followed will lead one deeply between the vessels. The question then arises regarding the exact location of the ductus and where dissection should be made to uncover it. There are three ways to determine the position of this vessel. (1) The ductus lies just opposite to or a little distal to the origin of the left subclavian artery. (2) The ductus may be compressed, and as this is done there will be a temporary disappearance of the thrill over the heart and pulmonary vessel. Thus, by running the finger along the sulcus, between the aortic arch and pulmonary artery, and pressing in various places, that point at which pressure stops the thrill will indicate the ductus site. (3) The left recurrent laryngeal nerve arises from the vagus nerve, courses downward, and then curves around the aortic arch a few millimeters posterior to the ductus. Hence the tracing of this structure will lead one directly to the ductus.

It has been my practice to quickly locate the general position of the ductus by finding the point opposite the origin of the subclavian artery and

then press in various places below the aortic arch until the thrill is temporarily stopped. Careful attention is then turned to the isolation of the recurrent nerve for two reasons (Figs 1 and 2). First, the entire extent of this structure must be identified in the operative field so that it is in view at all times and can be left uninjured. Second, the following of this nerve is the best way to accurately locate the ductus. I have spent as long as an hour in locating, freeing up, and tracing this nerve, for it is time well spent, and once it is brought into view, the remainder of the dissection seems to be on a safer and surer basis.

The release of tissue around the ductus should be accomplished by blunt dissection. In this way less bleeding is encountered from small veins in the region. The postero-medial aspect of the ductus cannot be visualized completely, but gentle dissection here with a half length or a right-angle clamp will safely separate the underlying left main bronchus. The ductus should not be cleaned off too much, for if a small amount of areolar tissue is left around the vessel it will serve as a padding to prevent cutting-in of the ligature when it is applied. In most cases this entire dissection will be extra-pericardial, but in Case 3 the sac had a very high reflection and was opened into. At this stage haste should be avoided because a too rapid dissection may stir up bleeding and produce ecchymoses through the tissues which obscure the field and hamper the remainder of the operation. The elapsed time of isolating the ductus after the opening of the pleura was in no case less than an hour and in the last patient consumed nearly two hours.

An aneurysm needle carrying the ligature material may now be passed around the ductus. Before permanently obliterating the vessel it is best to make a temporary occlusion for two or three minutes to insure that closure of the vessel will not in any way embarrass the circulatory apparatus. During this period the patient's color, blood pressure, pulse, and cardiac action can be observed for any untoward reactions. This temporary closure may be made by drawing up the thread and holding it with the fingers, or else the thread may be passed onto a Shenstone hilar tourniquet which is drawn up snugly without employing the ratchet (for fear of cutting through the ductus). If no undesirable effects are produced during the temporary observation period, the ductus may be permanently ligated. The ligature material

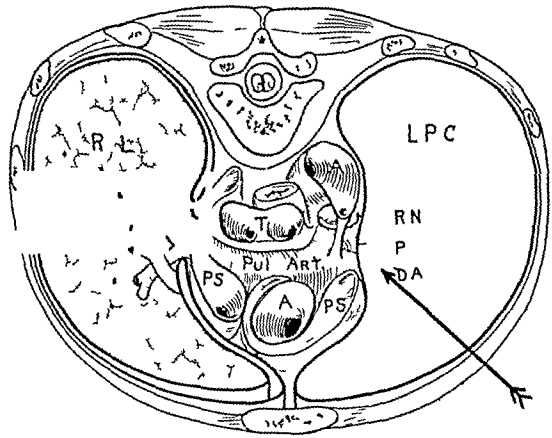


FIG 2—Sketch of a horizontal section through the fifth thoracic vertebra, showing route by which the ductus arteriosus may be exposed by an antero-lateral approach through the left chest. If the left pleural cavity (LPC) is opened, the lung collapses toward the inferior part of the chest. The operator can then look directly at the mediastinum and can expose the ductus by incising the parietal pleura (P). (A) Ascending and descending aorta. (DA) Ductus arteriosus. (Pul Art) Pulmonary artery. (PS) Pericardial sac. (RL) Right lung. (RN) Recurrent nerve. (T) Trachea, at its bifurcation. Arrow shows direction of operative approach through the left second or third intercostal space.

in all cases of the present series was No 8 heavy braided silk (Gudebrod Company) In two cases only one ligature was employed, but in the other patients two ligatures were used The latter is unquestionably a better practice, and it might be advisable to inject a few drops of sclerosing fluid into the ductus between the constricted points It cannot be emphasized too strongly that these ligatures must be drawn up *very tightly* if complete obliteration is to be effected When a satisfactory closure has been made there is *complete* disappearance of the thrill in the pulmonary artery

It would be a preferable surgical procedure to divide the ductus rather than ligate it in continuity, but in our series this was impossible because of the shortness of the vessel

The operative closure can now be completed rapidly The edges of the mediastinal pleura are approximated with continuous or interrupted sutures The cut ends of the costal cartilage are anchored to one another with a heavy catgut suture, piercing the cartilage with a sharp needle The intercostal muscles are approximated with continuous catgut, reexpanding the lung completely with positive pressure before the last suture is drawn up and tied The pectoral muscle is repaired with continuous catgut to the muscle fasciae and a few interrupted mattress sutures to butt together the ends of the muscle The subcutaneous fascia must be carefully sutured or there will be a marked tendency for the incisional scar to subsequently spread

Postoperative Care—There is remarkably little postoperative reaction In the first three cases eucupine solution was injected into the intercostal nerves while the chest was still open The prolonged anesthetic action of the drug appeared to greatly reduce postoperative discomfort in the wound In the first case, the child was allowed out of bed in a wheel chair on the first postoperative day (Fig 5) and was walking on the third day (Fig 6) The wounds all healed per primam There was some edema for three or four days, but there was no permanent collection of fluid such as was anticipated from cutting across the lymphatics of the breast (Fig 17) There was a moderate tendency for the skin wounds to spread and become conspicuously wide There was no difficulty with healing of the transected pectoral muscles after a regimen of immobilizing the upper arm for two or three weeks In two patients, fluid collected in the left pleural cavity, which was not aspirated and which was resorbed spontaneously in about ten days

Operative Results—There have been no important postoperative complications There has been no mortality in the cases thus far operated upon In every patient the thrill has disappeared In Cases 1 and 2 there is still a faint to-and-fro murmur at the pulmonic area, doubtless due to a small leak within the wrinkled spaces of the collapsed duct After these experiences, two ligatures were used in Cases 3 and 4 and this change in technic makes us feel certain that these ducts are completely obliterated for all murmurs have disappeared In every case there has been a restoration of the low, preoperative diastolic pressure to a normal level (Charts 2, 3, 4 and 5) In each case the overactive and forceful action of the cardiac impulse has been

reduced to one of normal intensity. The transverse dimension of the heart in Cases 1 and 2 did not change appreciably, but in Cases 3 and 4 it has decreased 1 cm and 0.5 cm, respectively. Case 2 had always complained of difficulty in gaining weight, but within four months after operation he has gained nine pounds. Each of these children has returned to school and bids fair to have an improved cardiovascular system.

In Cases 3 and 4 samples of blood (for oxygen content) were taken during operation from the aorta, the ductus, the main pulmonary artery, and the left pulmonary before and after ligation of the ductus. After determining the patient's oxygen consumption, it was then possible to calculate the volume of blood flowing to the periphery, through the ductus, and through the right and left sides of the heart. These studies are reported more fully elsewhere,⁷ but a few of the findings are listed here. In Case 3, the peripheral blood flow was 4.86 liters per minute while the ductus was still open and was increased to 6.12 liters per minute after the ductus was ligated. In Case 4, the peripheral blood flow was 5.8 liters per minute while the ductus was open. Concurrent with this peripheral flow, 18.8 liters of blood per minute passed through the ductus, making a total of 24.6 liters which the left ventricle had to pump per minute in order to maintain the peripheral flow at a normal level. Following ligation of the ductus, the left ventricular output was 5.08 liters per minute, and this entire amount was of course distributed to the periphery. In short, this heart was performing more than four times as much work as was necessary while the ductus was open. It is at once evident that ligation of the ductus greatly increases the cardiac efficiency, the increase in efficiency being dependent upon the size of the ductus which is obliterated. (The above figures all represent conditions with the patients under cyclopropane anesthesia, and while the figures are somewhat higher than in the unanesthetized individual, the general relationships are still true.)

The four patients thus far operated upon at the Children's Hospital and the Peter Bent Brigham Hospital are here presented in summarized form. Preliminary reports of these have been made previously^{11, 12, 13}

Case 1—L. S., female, age 7, entered the Children's Hospital, August 17, 1938, for study of her cardiac condition. At one and a half years of age her mother noted that the child was short of breath. At three years, examination, in another hospital, revealed findings of congenital heart disease. After having several epistaxes and episodes of pain in the extremities she was studied at four years of age in a second hospital. No evidence of rheumatic fever was found and there were no objective findings in the extremities. The discharge diagnosis was "patent ductus arteriosus." On entering school the child was bright and active, but often noticed that she could not play as long or as strenuously as did other children of her age. Frequently, she would stand still, have a rather frightened appearance, and would place her hand over her heart. When asked what was the trouble, she would whisper "something wrong inside of here." These apparently represented attacks of palpitation with momentary dyspnea. The mother volunteered the information that she "often heard a buzzing noise in the child's chest" when standing near her. At no time had there been cyanosis.

Physical Examination—The patient was 49 inches tall and weighed 48 pounds. She was below the average physical development for her age and was moderately undernourished (Fig 3). Inspection and auscultation showed a heaving, overactive cardiac impulse. There was a loud, to-and-fro machinery murmur accentuated during systole which was loudest over the pulmonic area, but was transmitted widely over the precordium and to a less extent to the axillae and back. A continuous thrill, greatest during systole, was felt along the left border of the sternum, particularly toward the base of the heart. Blood pressure 115/40.

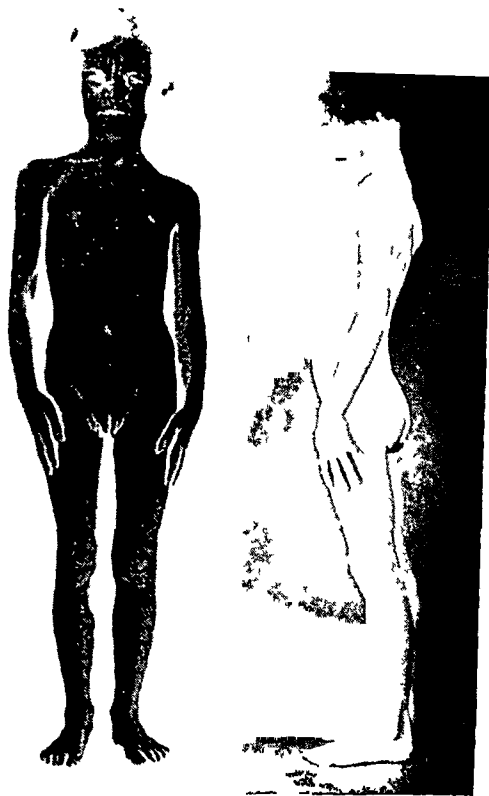


FIG 3—Case 1. Seven year old patient showing general body contour. Moderate undernourishment noted particularly in the prominence of the ribs.

Laboratory Data—Red blood count 5,080,000. Circulation time, right elbow to tongue, with Decholin, eight to 10 seconds. Seven-foot heart film (Fig 4) showed the heart to be enlarged with a transverse diameter of 11.7 cm compared to an internal chest diameter of 20.0 cm. The enlargement was mainly in the left ventricle, and the pulmonary artery was more prominent than normal. Considerable perihilar congestion was noted. Fluoroscopy demonstrated a definite "hilar dance" in the lung vessels, particularly on the right. Electrocardiograms were normal.

Operation—Artificial left pneumothorax was first performed to determine whether subsequent collapse of the lung during operation would seriously affect the patient. Inasmuch as there was no important reaction to this procedure, exploration was undertaken two days later.

On August 26, 1938, under cyclopropane anesthesia, an incision was made from the left sternal border to the left anterior axillary line just below the breast. The pectoral muscles were divided and the chest entered through the third left interspace after cutting the third costal cartilage. As the lung collapsed a good view of the heart and lateral aspect of the mediastinum was obtained. A very vibrant thrill was felt over the entire

SURGERY OF DUCTUS ARTERIOSUS

heart and the pulmonary artery After incising the pleural covering of the mediastinum and carefully dissecting below the aortic arch, a ductus 8 Mm in diameter and 5 Mm long was exposed This was ligated with a single, heavy, braided-silk ligature The

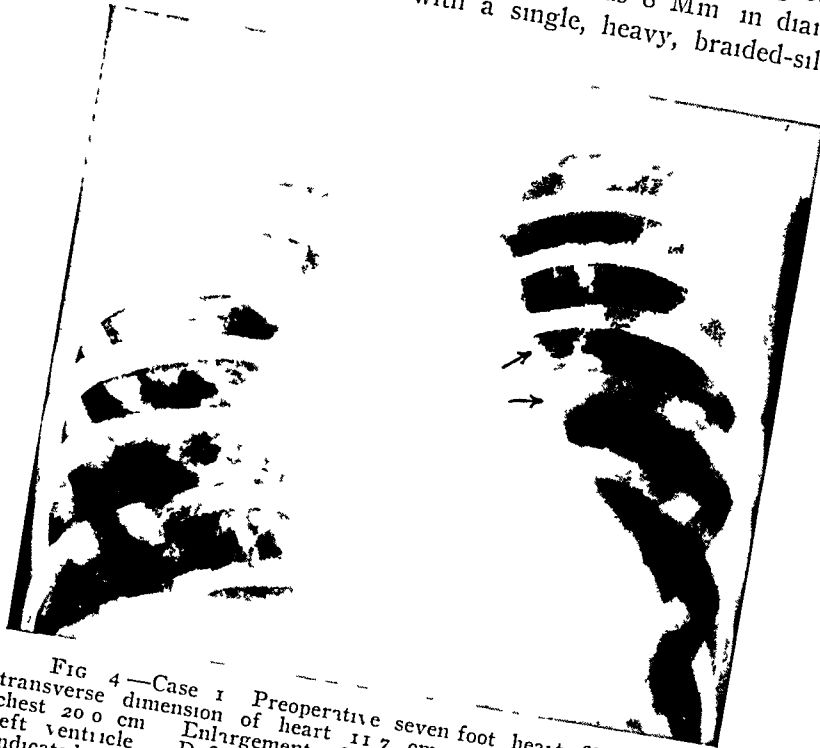


FIG 4—Case 1 Preoperative seven foot heart film Total transverse dimension of heart 11.7 cm Internal diameter of chest 20.0 cm Enlargement of heart, particularly in region of left ventricle Definite fulness in area of pulmonary artery, indicated by arrows Increased lung markings from vascular congestion, especially in right lung



FIG 5—Case 1 Photograph taken 24 hours after operation, showing patient out of bed and sitting up in a wheel chair There was little postoperative reaction



FIG 6—Case 1 Photograph on third postoperative day when patient was ambulatory, showing early recovery from the operative procedure Left arm is still immobilized in the dressing



FIG 7—Case 1 Photograph two months after operation showing position of the operative wound. Some weight gain is already seen in the fullness of the chest, compared to the prominent ribs in Figure 3

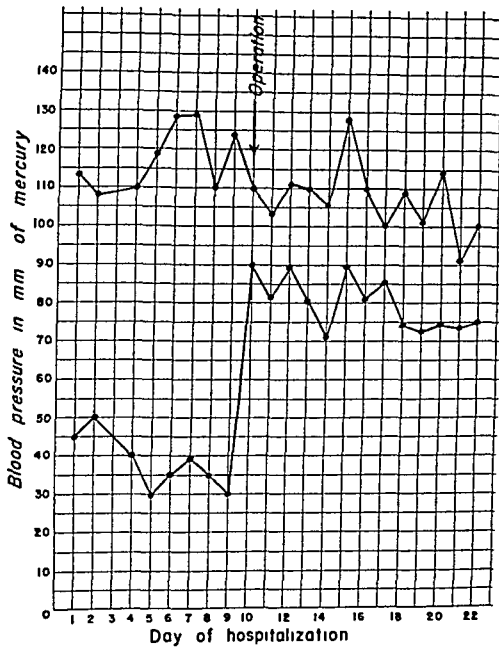


CHART 2—Case 1 Daily blood pressure chart during hospitalization showing the low diastolic level prior to operation and the immediate rise of the diastolic pressure following operative ligation of the ductus. Average daily diastolic pressure prior to operation was 38 Mm of Hg. Diastolic pressure at time of hospital discharge was 73 to 75 Mm of Hg.

thrill completely disappeared after closing the ductus. The mediastinal pleura was now sutured and, after the lung was reexpanded with positive pressure, the chest was closed.

Postoperative Course—There was very little postoperative reaction. The child was allowed out of bed and up in a wheel chair 24 hours after operation (Fig 5) and on the third day she was walking around the ward (Fig 6). The wound healed well except for some keloid formation (Fig 7). She was discharged on the thirteenth postoperative day. Examinations of the heart after operation and after hospital discharge showed the thrill to have disappeared. The cardiac action was now of normal intensity in contrast to its previous overactivity. There was a faint to-and-fro, soft murmur at the base, the systolic element of which was transmitted to the apex but not elsewhere. The diastolic

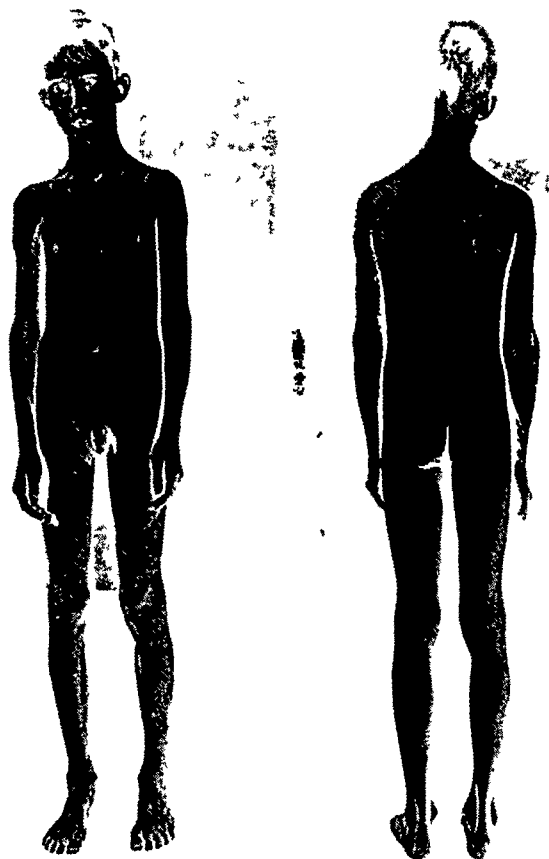


FIG 8—Case 2. Eleven year old boy with under development and deficient nourishment. Note the long thin extremities and fingers. Patient had great difficulty in gaining weight despite many years of clinic treatment.

blood pressure rose immediately on ligation of the ductus and has permanently remained normal at about 35 Mm of mercury above her preoperative level (Chart 2). Electrocardiograms six months after operation show no change. The child has returned to school, is active, and is gaining weight.

Case 2—R. C., male, age 11, entered the Children's Hospital, September 6, 1938. In the first year of life it was found that he had "heart trouble." Because of failure to gain weight he was first seen in the outpatient department at four years of age, at which time there was considerable malnourishment. At that examination, physical and roentgenologic findings were characteristic of a patent ductus arteriosus. On the present admission the child's chief complaint was that he was "always tired ever since he was big enough to run around." The child had noticed that he could never run and exercise as freely as his playmates. Exercise was never accompanied by cyanosis, but it

always brought on cardiac palpitation. The patient had never been able to gain weight properly in spite of guidance from the clinic.

Physical Examination—The boy was thin and distinctly undernourished (Fig 8). He was 58 inches high and weighed 62.5 pounds. The very forceful action of the heart imparted a marked pulsation to the anterior chest wall. A very loud and harsh, roaring continuous murmur, increased during systole, was heard in the pulmonic area. This was transmitted widely over the precordium, but the diastolic element was faint at the apex compared to the rather loud systolic apical murmur. The coarse systolic murmur could be heard in both axillae, particularly the left, over the back of the chest, but only faintly



FIG 9—Case 2. Seven foot roentgenogram prior to operation. Cardiac enlargement, particularly in region of left ventricle. Prominence of pulmonary artery indicated by arrows. Total transverse dimension of heart 11.3 cm. Internal diameter of chest 21.3 cm.

over the neck vessels. A vibrant, continuous thrill was felt over the precordium, especially in the left second and third interspaces. The pulmonic second sound was greatly increased. The blood pressure was 115/45. There was a definite Corrigan's pulse and a capillary pulsation in the fingernail beds.

Laboratory Data—Roentgenologically, the heart was enlarged, the transverse dimension being 11.3 cm compared to an internal chest diameter of 21.3 cm (Fig 9). Most of the cardiac hypertrophy appeared to be in the left ventricle. The pulmonary artery was prominent and the lung markings were increased. Electrocardiogram was normal. Red blood count 5,050,000.

Operation—September 12, 1938. Under cyclopropane anesthesia, a slightly curved incision, running from the left sternal border to include the left anterior axillary fold, was made just beneath the breast, transecting pectoral muscles and retracting breast and muscles upward. The thorax was entered in the third interspace, cutting the third costal

SURGERY OF DUCTUS ARTERIOSUS

cartilage The collapsed lung was protected with a gauze pack and the mediastinum was viewed from its left lateral aspect (Fig 10) A very coarse thrill was felt over the entire heart and pulmonary artery This was so marked that it tickled the operator's fingers while working in the region and touching the great vessels with forceps or other instruments The left recurrent laryngeal nerve was easily exposed Following this structure forward and medially, an enormous patent ductus, 11 or 12 Mm in diameter and 12 Mm in length, was found Attempts were now made to pass an aneurysm needle around the vessel so that ligatures might be brought into place In the performance of

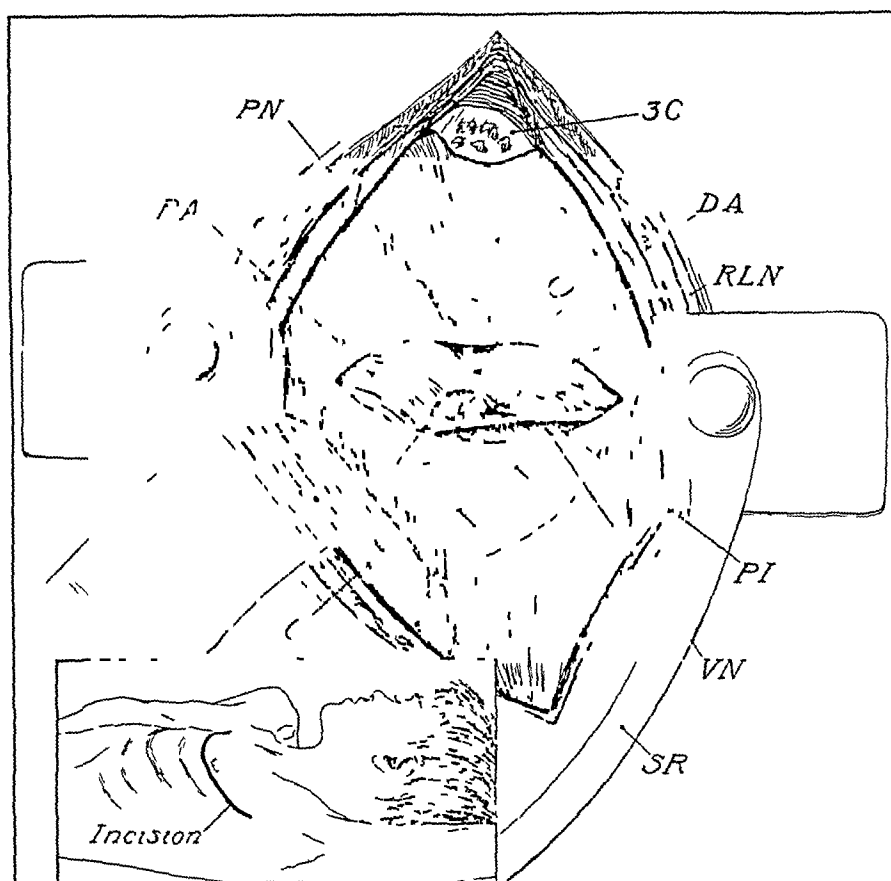


FIG 10—Case 2 Sketch of operative exposure of the ductus which was 11 Mm in diameter Insert shows position of patient with left arm drawn up along the head and with incision coursing just beneath the breast Thorax entered through the third interspace Third cartilage cut to allow upward retraction of ribs The left lung is held down inferiorly with a gauze pack and malleable retractor Positions of aorta and pulmonary artery indicated by dotted lines When the pleural covering of the mediastinum was incised a direct view of the aortic arch, pulmonary artery, and ductus was obtained (3C) Cut end of third costal cartilage (DA) Ductus arteriosus (G) Gauze pack over collapsed lung (PA) Pulmonary artery (PI) Pleural incision (PN) Phrenic nerve (RLN) Recurrent laryngeal nerve (SR) Self-retaining retractor (VN) Vagus nerve

this task the thin-walled ductus tore and there was a serious hemorrhage which bid fair to end the operation fatally However, a finger was held over the rent while a transfusion was finished and then with one finger over the hole, dissection was continued until ligature material could be carried around the ductus and tied up tightly Fortunately, all bleeding was thereby controlled After reexpanding the lung the chest was rapidly closed

Postoperative Course—Except for some discomfort in the wound for several days, requiring sedatives, there was little postoperative reaction On the fourth day, the patient was allowed out of bed and at the end of a week was walking He was discharged, September 29, 1938 The greatly accentuated cardiac beat has returned to normal activity The thrill has disappeared There is a to-and-fro murmur at the base which is soft, and

at times the diastolic element of this cannot be heard. The diastolic blood pressure has averaged about 30 Mm of mercury higher after operation, compared to its preoperative level (Chart 3). Roentgenograms of the chest two months after operation show no essential change in size or contour of the heart. The boy's general condition has gradually and definitely improved, there being a weight gain of nine pounds in the first four months after operation.

Case 3—F S, female, age 7, entered the Children's Hospital, November 2, 1938. During the first four years of life, she was always under normal weight. At three years of age, there was a loud cardiac murmur and a widespread coarse precordial thrill. These findings, with a blood pressure of 110/40, plus a Corrigan's pulse, led to a diagnosis of aortic stenosis and regurgitation. From the fourth to sixth year of life the child

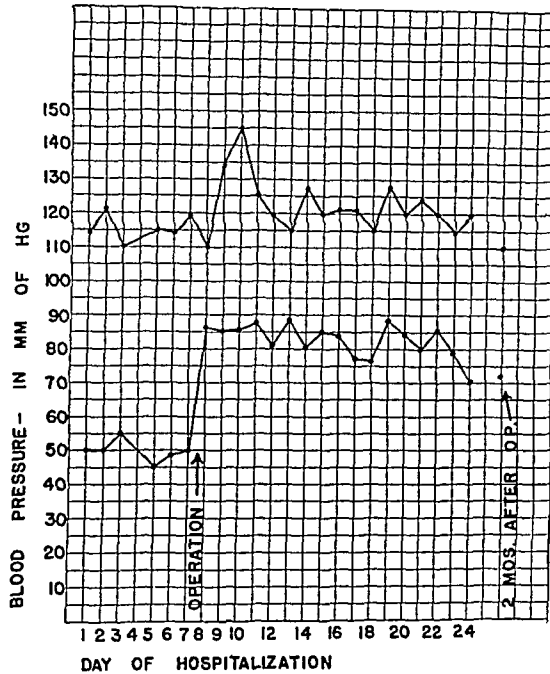


CHART 3—Case 2. Daily blood pressure during hospitalization. Low diastolic pressure which existed prior to operation was immediately restored to a normal level by ligation of the ductus. This increased diastolic level was maintained as indicated by the reading two months after operation.

was usually unstable, tired easily, had moderate dyspnea and chest pain on exertion, and dilated veins were often noticed over the anterior chest wall. Her general activity, however, was not greatly retarded. There had never been cyanosis.

Physical Examination—The patient was pale, somewhat thin and underdeveloped. The height was 46 inches and the weight 42.5 pounds. There was no cyanosis or clubbing. There was a marked precordial pulsation indicating a very active heart beat. There was an intense and coarse thrill over the entire precordium, most vibrant in the third left interspace, which was more pronounced in systole but which extended into diastole. A loud rough systolic murmur was heard in the pulmonic area which was transmitted over the entire precordium and with considerable intensity to both axillae and the back. In the pulmonic area there was also an untransmitted diastolic murmur which produced a to-and-fro, continuous murmur at the base. P_2 was greatly accentuated. The blood pressure was 115/50.

Laboratory Data—Red blood count 5,090,000. Electrocardiograms were negative except for splintering of the QRS complex in Lead 3 (Graph 1). Roentgenograms and fluoroscopic examination of the heart showed slight enlargement to the left (Fig 11).

SURGERY OF DUCTUS ARTERIOSUS

Transverse dimension of the heart 9.8 cm, compared to an internal diameter of the thorax of 18.6 cm. There was a marked bulge in the region of the pulmonary artery and also considerable pulsation of the congested pulmonary arteries. Blood volume was 1,600 cc as determined by the Gibson⁸ method.

Operation—November 9, 1938. Under cyclopropane anesthesia, the same general approach as in Cases 1 and 2 was employed, but incision was made above the breast, and the second as well as the third costal cartilages were cut. When the chest was opened in the third intercostal space, a very wide and satisfactory exposure of the heart and superior mediastinum was obtained. The heart had a very forceful impulse and there was a marked thrill over the entire organ and over the pulmonary artery. After considerable time-consuming dissection, which required opening of the superior portion of the



FIG. 11.—Case 3. Seven foot roentgenogram prior to operation. Moderate cardiac enlargement. Prominence in region of pulmonary artery indicated by arrows. Increased markings in lung fields. Total transverse dimension of heart 9.8 cm. Internal diameter of chest 18.6 cm.

pericardial sac, the underportion of the aortic arch was bared and the ductus was found to be 7 mm in diameter and 7 to 8 mm long (Fig. 12). After a preliminary pinching-off of the ductus for three minutes, to make sure there would be no deleterious effects, the vessel was permanently obliterated with two heavy braided and waxed silk ligatures. The thrill disappeared immediately, the diastolic pressure in the arm rose greatly, and the heart slowed (within two or three beats) from 100 to 70. This latter very prompt and dramatic response was probably brought about by the raising of pressure in the aortic arch which slowed the heart reflexly by way of the cardiac depressor nerve. The pulmonary artery, which prior to ligation had been quite tense, was distinctly softer after closure of the ductus. Two silver clips were placed on one of the ligatures so that this region might be accurately identified in postoperative roentgenograms (Fig. 14). The lung was then reexpanded with positive pressure and the chest closed.

Postoperative Course—The wound healed well and the patient was discharged on the thirteenth postoperative day (Fig. 13). Like the other patients operated upon with

this approach, there was no disability from section and suture of the pectoral muscles. The heart, which had been so active prior to operation, now had a beat of normal intensity. The thrill has disappeared and absolutely no murmurs can now be heard. The diastolic blood pressure showed a marked change. Before operation this had varied from 30 to 50, and beats could be heard all the way down to zero. After operation the diastolic pressure was almost constantly at 80 and no beats could be heard below 65 or 70 (Chart 4). Postoperative electrocardiograms showed no change (Graph 1). Reexamination of

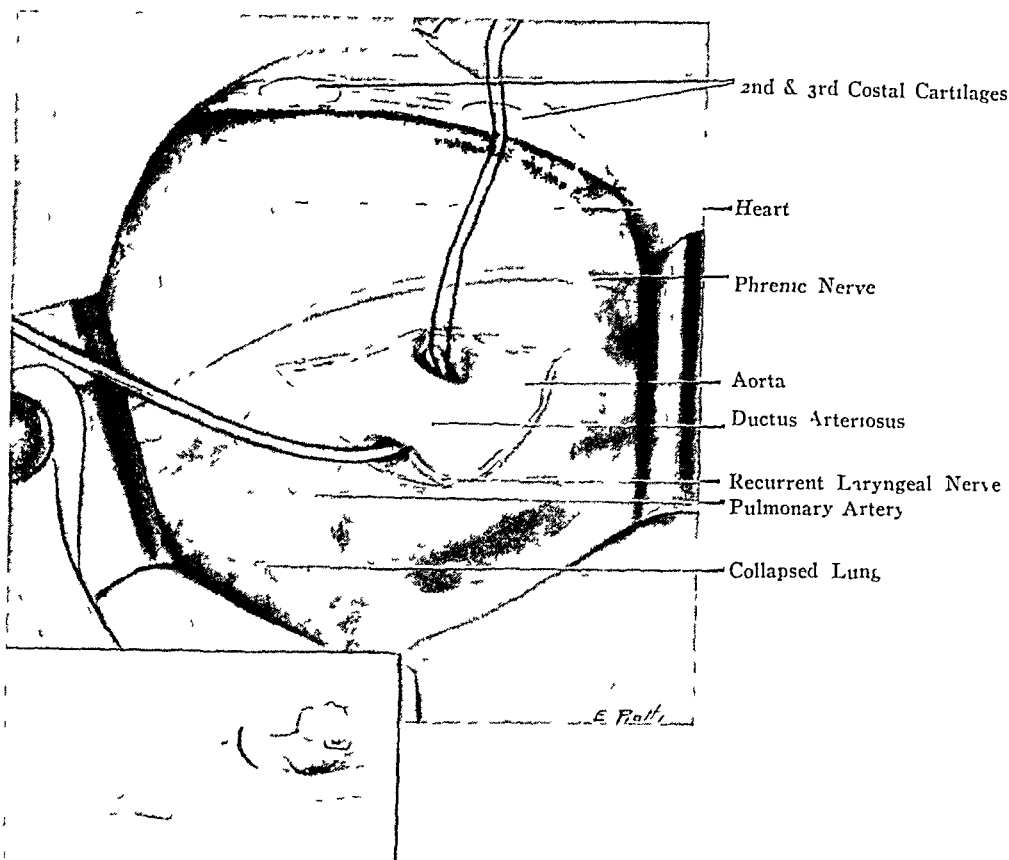


FIG 12—Case 3. Operative exposure of patent ductus arteriosus which was 7 Mm in diameter. Incision of pleura made posterior to the phrenic nerve. After dissecting fatty and areolar tissue from the sulcus between aortic arch and pulmonary artery, the recurrent laryngeal nerve and the ductus were brought into view. The origin of the left subclavian artery is just seen on the aortic arch, opposite to and a little proximal to the ductus opening. Aneurysm needle passed around the ductus. Second and third costal cartilages both cut in this case. Insert shows position of the skin incision which in this patient was made above the breast.

the heart, two months after operation, showed the left auricle to be smaller and there was a diminution in the transverse dimension of the heart of 1 cm (Fig 15). Kymograms also showed diminished ventricular excursions after operation. Of particular interest was the pulmonary artery, which had collapsed but little as viewed in the roentgenogram. However, by kymogram, this vessel as well as the aortic knob was seen to pulsate much less than before operation (Graph 2). The child's general condition has been excellent, she has returned to school and in the first two months after operation she has gained three pounds in weight.

Case 4—M. F., female, age 17, entered the Peter Bent Brigham Hospital, November 28, 1938, for study of her cardiac condition. At the age of three, a cardiac murmur was first discovered. At the age of five, she entered another hospital for treatment of marked cardiac decompensation and at that time was hospitalized for six months.



FIG 13—Case 3 Photograph showing position and condition of wound on tenth postoperative day



FIG 14—Case 3 Roentgenogram of heart following operation to show position of the two silver clips which were placed on the ductus ties to identify this region The obliterated ductus is a few millimeters medial to these clips

During that time her general condition gradually improved. From the age of six until 12 there were frequent and very copious epistaxes. Except for occasional dyspnea there was little limitation of her physical activity, but the child noticed that she always tired more easily than her playmates. After entering high school increased physical exertion

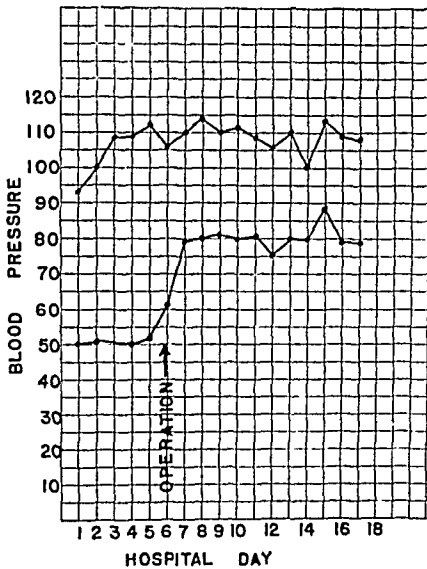
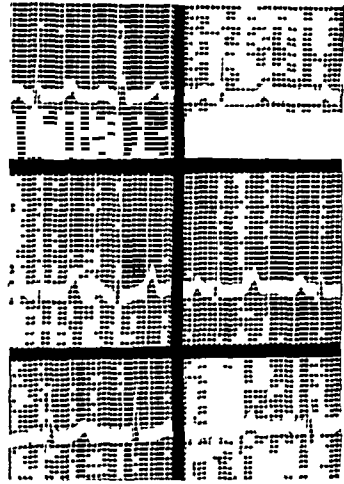


CHART 4—Case 3. Daily blood pressure chart indicating marked change in the diastolic level after obliteration of the patent ductus.



GRAPH 1—Case 3. Electrocardiograms before operation on left, and after operation on right. Normal curves before operation. No important change after operation.

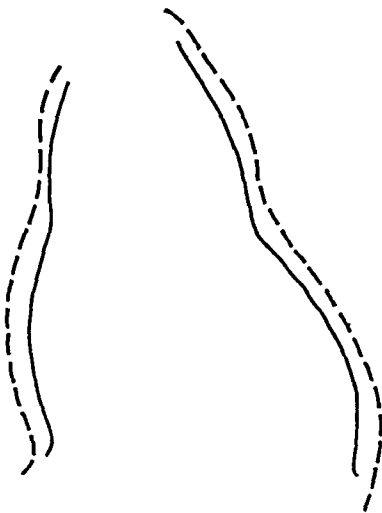
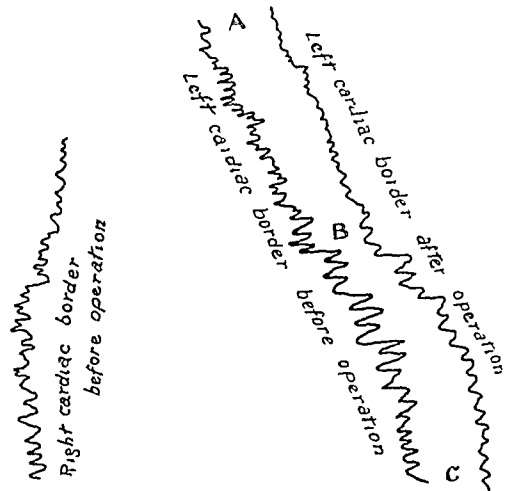


FIG 15—Case 3. Outlines of heart before operation (dotted line) and after operation (solid line) as traced from seven foot heart films showing reduction in size of heart following closure of the aorto pulmonary artery shunt. Transverse diameters 9.8 cm and 8.8 cm before and after operation, respectively.



GRAPH 2—Case 3. Tracings taken from preoperative kymogram of heart to compare with postoperative tracing of left cardiac border. Prior to operation there was an increased amplitude of movement in the left ventricular border which is reduced after operation. Prior to operation there was marked pulsation in the aortic knob and pulmonary artery regions which is greatly reduced after ligation of the ductus. (A to B) Region of aortic knob and pulmonary artery. (B to C) Border of left ventricle.

brought recurring episodes of moderate decompensation so that the curriculum had to be greatly reduced. On several occasions she was in bed from one to three months. During these periods of incapacitation there was swelling of either or both legs, accompanied by dyspnea. For the year prior to hospitalization formal schooling had to be abandoned, and the patient was kept at home. For two months prior to hospital entry there had been

SURGERY OF DUCTUS ARTERIOSUS

three or four attacks of gripping pain in the left chest which were relieved by rest. During this time there had been moderate orthopnea and frequent palpitation. For several years there had been frequent attacks of tonsillitis and at times the question of rheumatic fever had been raised, though there was no swelling, tenderness, or increased heat of the joints at any time.

Physical Examination—The patient was a small-framed, thin, somewhat undernourished individual weighing 95 pounds. The general physical condition was good. The tonsils were enlarged and mildly inflamed. The thorax was a little more prominent on the left than on the right. The lungs were clear. The cardiac action was extremely forceful, even during rest in bed. Over the pulmonic area was a loud, coarse, continuous machinery murmur with systolic accentuation. This was transmitted widely over the



FIG 16—Case 4. Seven foot heart film before operation. Moderate cardiac enlargement. Transverse dimension of heart 12.8 cm. Internal diameter of chest 24.0 cm. Prominence of pulmonary artery indicated by arrows. Just below this is slight fulness in region of left auricle. Vascular congestion throughout lung fields.

precordium, to both axillae and over the back, but was only faintly heard over the neck vessels. At the cardiac apex the systolic element of the murmur appeared to be of the same character as that at the base, but the diastolic component had a different quality. The second pulmonic sound was greatly accentuated. A continuous thrill with systolic accentuation was felt over the pulmonic region. The blood pressure was 124/60.

Laboratory Data—Roentgenologic examination of the heart showed moderate cardiac enlargement, chiefly left ventricular hypertrophy with slight fulness of the pulmonary artery (Fig 16). There was considerable enlargement of the left auricle, particularly in its posterior portion. In the hilum the pulmonary vessels were slightly dilated. Fluoroscopy showed a very vigorous beat. Transverse dimension of the heart was 12.8 cm compared to an internal diameter of the chest of 24.0 cm. The vital capacity was 1,800 cc. Venous pressure was 86 Mm of water. Circulation time, antecubital fossa to tongue,

was increased to 22 seconds Red blood count 4,940,000 Blood volume by the Gibson technic was increased to 3,950 cc

There was some question in this case concerning the presence of a complicating mitral stenosis which might be masked by the prominent signs of the patent ductus, but it was felt that the patient's cardiac reserve could be greatly improved by ligating the ductus

Operation—December 22, 1938 Under cyclopropane anesthesia, a transverse incision was made just above the breast, dividing the pectoralis major and minor muscles and entering the chest in the second interspace after dividing the second costal cartilage When the lung was packed away inferiorly an excellent exposure of the aortic arch and pulmonary artery was obtained After opening the pleural covering of the mediastinum, a vascular and quite dense meshwork of fat and areolar tissue was found in the sulcus between the great vessels Nearly two hours were consumed in carefully dissecting this



FIG 17—Case 4 Postoperative photograph to show position of the operative incision This transverse section of the supramammary structures and the pectoral muscles does not produce any clinical evidence of impaired lymphatic drainage of the breast

area in order to avoid hemorrhage The ductus was finally exposed and was found to be 8 to 9 Mm in diameter and 5 to 6 Mm in length The vessel was firmly occluded with two No 8 braided silk ligatures The marked thrill which was previously felt over the entire heart and over the pulmonary artery now completely disappeared The heart, which had previously been very vigorous and overactive, immediately assumed a quiet and normal pulsation The diastolic blood pressure immediately increased 25 Mm of mercury There were no untoward effects from ligating the ductus During the operation samples of blood for oxygen content determinations were taken from the aorta and the pulmonary artery before and after ligation of the ductus in order to study the blood flow through the greater and lesser circuits⁷ The pleural covering of the great vessels was repaired and the chest closed after reexpanding the lung with positive pressure

Postoperative Course—There was a mild febrile reaction for four days, following which the temperature was normal There was some collection of fluid in the left chest which was not aspirated and which disappeared in ten days The wound healed *per*

SURGERY OF DUCTUS ARTERIOSUS

primam (Fig 17) The patient was discharged in excellent general physical condition on the sixteenth postoperative day. The cardiac impulse has assumed a normal intensity. The thrill has disappeared. No murmurs can be heard at the apex. A very faint and soft systolic murmur could be occasionally heard over the pulmonic region for three to four weeks, but this has now completely disappeared. The systolic blood pressure has changed very little, but the diastolic pressure has a sustained increase of 25 to 30 Mm of mercury above the preoperative level (Chart 5). Roentgenologic examination, two weeks after operation, showed a definite decrease in the total transverse diameter of the heart of

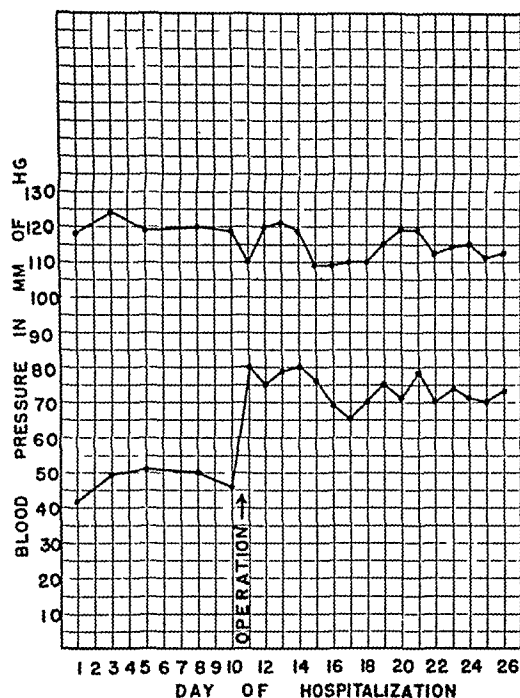


CHART 5—Case 4. Blood pressure chart during hospitalization. Low diastolic pressure before operation compared to normal diastolic after operation.

0.5 cm. There has been a change in the contour of the heart, with a decrease in the size of the left auricle. There is only slight decrease in the size of the pulmonary artery but the vessel has greatly decreased pulsations on kymographic tracings. The intrapulmonary vessels are definitely smaller and sharper. Reexamination, two months after operation, shows the blood volume to be reduced to a normal value of 3,280 cc, the circulation time to be reduced to a normal of 12 seconds, and the vital capacity to be increased.

SUMMARY AND CONCLUSIONS

The ductus arteriosus has a normal function of shunting blood from the pulmonary artery to the aorta while the lungs are collapsed before birth. If the ductus does not spontaneously close in the first year of postnatal life, the patient is left with a vascular fistula which then permits blood to escape in large quantities from the aorta to the pulmonary circuit. The presence of such a patent ductus is compatible with a long and active life, but it carries with it an increased likelihood of superimposed bacterial endarteritis or of cardiac decompensation resulting from what is essentially an arteriovenous aneurysm.

Surgical obliteration is advocated as a method of avoiding the complica-

tions to which the possessor of a patent ductus is liable. The operative steps for accomplishing this task were studied on postmortem material, were practiced on dogs, and are described herewith. The ductus can be adequately exposed by an approach through the left pleural cavity, entering the superior mediastinum from its left lateral aspect.

The feasibility of this operative procedure is demonstrated by the report of four patients upon whom it was performed without mortality or complications. These results indicate that the ductus can be explored with safety and that it can be permanently ligated in most instances. The success which has thus far been encountered in these surgically treated cases makes it important to recognize the condition, for surgery has much to offer these individuals. When there are no serious complicating cardiovascular lesions, surgical closure of the ductus can be performed with low risk and should ward off the dangers of subacute bacterial endocarditis and cardiac failure.

BIBLIOGRAPHY

- ¹ Abbott, M. E. Congenital Heart Disease. Nelson's Loose Leaf Living Medicine. Thomas Nelson, New York, 4, 207.
- ² Barclay, A. E., Barcroft, J., Barron, D. H., and Franklin, K. J. X-ray Studies of the Closing of the Ductus Arteriosus. *Brit J Radiol*, 11, 570, 1938.
- ³ Bohn, H. Ein Wichtiges Diagnostisches Phänomen zur Erkennung des Offenen Ductus Art Botalli. *Klin Wchnschr*, 17, 907, 1938.
- ⁴ Chester, W. Patent Ductus Botalli with Subacute Bacterial Endocarditis and Recovery. *Am Heart J*, 13, 492, 1937.
- ⁵ Christie, A. Normal Closing Time of the Foramen Ovale and the Ductus Arteriosus. *Am J Dis Child*, 40, 323, 1930.
- ⁶ Dry, D. M. Congenital Aneurysmal Dilatation of Ductus Botalli. *Am J Dis Child*, 22, 181, 1921.
- ⁷ Eppinger, E. C., Burwell, C. S., and Gross, R. E. Dynamics of the Circulation in Patients with Patent Ductus Arteriosus. To be published.
- ⁸ Gibson, J. G., and Evans, W. A. Clinical Studies of the Blood Volume. I. Clinical Application of a Method Employing the Azo Dye "Evans Blue" and the Spectrophotometer. *J Clin Invest*, 16, 301, 1937.
- ⁹ Graybiel, A., Strieder, J. W., and Boyer, N. H. An Attempt to Obliterate the Patent Ductus Arteriosus in a Patient with Subacute Bacterial Endarteritis. *Am Heart J*, 15, 621, 1938.
- ¹⁰ Gross, R. E. A Surgical Approach for Ligation of a Patent Ductus Arteriosus. *New England J M*, 220, 510, 1939.
- ¹¹ Gross, R. E., and Hubbard, J. P. Surgical Ligation of a Patent Ductus Arteriosus. Report of First Successful Case. *J A M A*, 112, 729, 1939.
- ¹² Gross, R. E., Emerson, P., and Green, H. Surgical Exploration and Closure of a Patent Ductus Arteriosus. Report of Second Successful Case. *Surgery*, in press.
- ¹³ Gross, R. E., Emerson, P., and Green, H. Surgical Obliteration of a Patent Ductus Arteriosus in a Seven-Year-Old Girl. *Am J Dis Child*, in press.
- ¹⁴ Holman, E. Certain Types of Congenital Heart Disease Interpreted as Intracardiac Arteriovenous and Venoarterial Fistulae. Patent Ductus Arteriosus. *Bull Johns Hopkins Hosp*, 36, 61, 1925.
- ¹⁵ Mallory, T. B. Case Records (No 24222) of the Massachusetts General Hospital—Patent Ductus Arteriosus with Subacute Bacterial Endocarditis. *New England J M*, 218, 937, 1938.

- ¹⁶ Matusoff, I Congenital Mirror Picture Dextrocardia with Situs Transversus, Patent Ductus Arteriosus and Subacute Bacterial Inflammation *Am J Dis Child*, 39, 349, 1930
- ¹⁷ Moench, G L Aneurysmal Dilatation of Pulmonary Artery with Patent Ductus Arteriosus Death from Rupture of Aneurysm into Pericardial Sac *J A M A*, 82, 1672, 1924
- ¹⁸ Muir, D C, and Brown, J W Patent Ductus Arteriosus *Arch Dis Child*, 7, 291, 1932
- ¹⁹ Munro, J C Ligation of the Ductus Arteriosus *ANNALS OF SURGERY*, 46, 335, 1907
- ²⁰ Patten, B M The Changes in Circulation Following Birth *Am Heart J*, 6, 192, 1930
- ²¹ Perry, C B Patent Ductus Arteriosus, with Superimposed Subacute Bacterial Endocarditis *Lancet*, 1, 82, 1933
- ²² O'Shaughnessy, L Personal Communication
- ²³ Scammon, R E, and Norris, E H A Statistical Summary of the Data on the Time of Obliteration of the Foramen Ovale, Ductus Arteriosus, and Ductus Venosus in Man *Anat Rec*, 15, 165, 1918
- ²⁴ Schaeffer, J P The Behavior of Elastic Tissue in the Postfetal Occlusion and Obliteration of the Ductus Arteriosus (Botalli) in Sus Scrofa *J Exper Med*, 19, 129, 1914
- ²⁵ Schlaepfer, K Chronic and Acute Arteritis of the Pulmonary Artery and of the Patent Ductus Arteriosus *Arch Int Med*, 37, 473, 1926
- ²⁶ Schrotter, H von Über eine seltene Ursache einseitiger Recurrenslähmung, zugleich ein Beitrag zur Symptomatologie und Diagnose des offenen Ductus Botalli *Ztsch f klin Med*, 43, 160, 1901
- ²⁷ Trimble, W H, and Larsen, R M A Case of Patent Ductus Arteriosus with Primary Bacterial Pulmonary Endarteritis *Am Heart J*, 6, 555, 1931
- ²⁸ Wessler, H, and Bass, M H Persistent Ductus Botalli and Its Diagnosis by the Orthodiagraph *Am J Med Sci*, 145, 543, 1913

DISCUSSION—DR. MONT R. REID (Cincinnati, Ohio) I am sure that I voice the feelings of the members of the American Surgical Association when I express my admiration for this splendid and brilliant paper, we are truly grateful to you, Doctor Gross. There can be no doubt that you have made an enduring contribution to the knowledge and art of surgery. That others have thought of and tried unsuccessfully to do what you have reported here to-day, in no way detracts from the careful and painstaking studies you have just recited. That is the common experience of all of us and it is rather to your credit that you were not deterred by the failures of others.

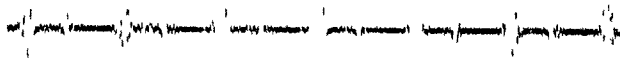
Permit me also to admire the words of caution with which you have surrounded this obvious advance in surgery. If the operation which you have so successfully employed in four cases should for a time become discredited by misuse, it will be no fault of yours. From your laboratory and clinical investigations you have laid down certain rules or standards of procedure which should be our guiding principles until further experience or study warrants a change in them. That changes will come is inevitable, but to have this work discredited by hasty or unwise use would be deplorable.

Having in mind the criteria of operability which you have proposed, I have reviewed the records of 15 living cases of patent ductus arteriosus. Of these, 11 appear to be uncomplicated by other abnormalities, two, to have patent interventricular septa, and two, to have pulmonary stenosis. Of this entire number, only one appears to satisfy fully your requirements for operative intervention. He is a poorly nourished boy, age 11, exhibiting the typical murmur and thrill, the accentuated pulmonary conus, left ventricular enlargement, low diastolic pressure, free of evidence of other cardiac defects, dyspnea,

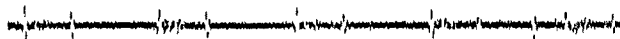
and no evidence of bacterial endarteritis. There are two other cases which almost meet your criteria of operability. In this series, there is one child, who at the age of six met all of your requirements but who now, at the age of



NORMAL SOUND TRACING



PATENCY OF DUCTUS ARTERIOSUS



CONGENITAL ARTERIOVENOUS ANEURYSM

GRAPH 1—Sound tracings of a normal heart, a heart with patent ductus arteriosus, and of a congenital cirroid aneurysm

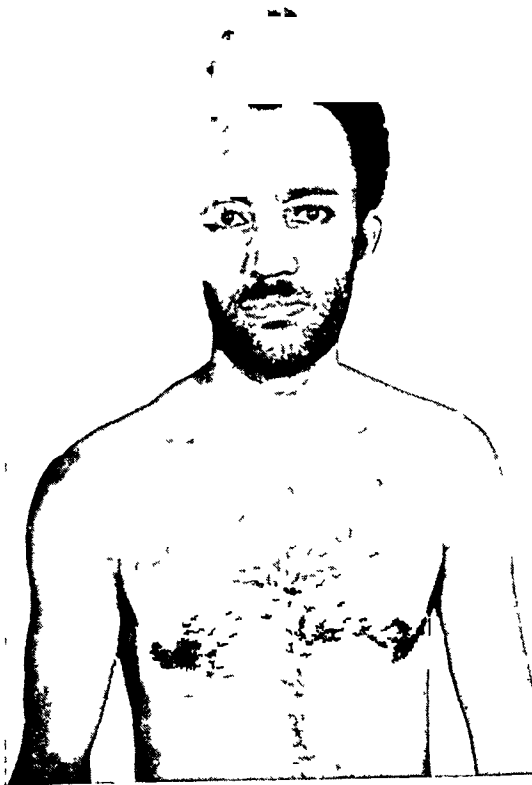


FIG 1—A 33 year old colored man with patent ductus arteriosus, with typical clinical findings, and in apparently excellent health

15, appears to be perfectly well, although the ductus is open. Should we operate? On the other hand, another patient who, at the age of three, seemed, by your standards, to justify an operation, is now, at the age of seven, dying

SURGERY OF DUCTUS ARTERIOSUS

from bacterial endarteritis. In view of Hamman's experience with a malignant vegetative arteritis at the site of an arteriovenous fistula, I cannot help but question your logic in refusing to operate for a vegetative lesion in association with a patent ductus arteriosus. There seems, undoubtedly, to be a causal relationship between patent ductus arteriosus and the occurrence of vegetative endarteritis, and it appears logical to me to hope that the surgical elimination of the patent duct might have some beneficial effect in promoting the healing of the vegetative lesion.

TABLE I

SUMMARY OF 15 LIVING CHILDREN WITH CLINICAL DIAGNOSIS OF PATENT DUCTUS ARTERIOSUS

	Primary Lesion	Other Complicating Defects	
		Patent Interventricular Septum	Pulmonary Stenosis
No. of cases	11	2	2
Age range—1 to 16 years			
Average time followed— 4 years 5 months			
Cyanosis			
Slight	3	0	0
Moderate	0	2	1
Exertion dyspnea			
Slight	3	0	1
Moderate	2	0	0
Marked	0	0	1
Peripheral edema	1	0	0
Delayed development	2	1	1
Clubbed fingers	1	0	0
Precordial bulging	1	0	0
Corrigan's pulse	0	0	1
Low diastolic pressure	4	1	1
Systolic thrill	3	1	0
Murmur			
Typical	11	2	1
Systolic	0	0	1
X-ray			
L V enlargement	8	2	1
Accentuated pulmonary conus	4	1	0
Abnormal EKG	0	0	2
Restricted activity required			
Moderate	3	2	1
Marked	1	0	1
Living	10	2	2
Case developed bacterial endocarditis at age seven	1 (probably dead)	0	0
Cases satisfying criteria for operation			
Definite	1	1	0
Probable	2	0	0

In a series of 8,300 autopsies, performed at the Cincinnati General Hospital, there are recorded 489 instances of patent ductus arteriosus. Of these, 231 were noted in stillborn infants and are, therefore, of no significance.

There were, however, 258 cases in which death occurred after birth. Of this number, 176 deaths occurred within one week and all, except one, within eight months. On analyzing the causes of death, I was impressed by the very high incidence of pulmonary atelectasis. This is an interesting observation, although I am not prepared to discuss its significance. There was one girl who died from a brain abscess at the age of 14. The clinical history was typical of a bacterial septicemia, although at autopsy no vegetative endarteritis was noted at the site of the patent ductus.

We now have under observation a colored man, age 33, who has a typical patent ductus arteriosus (Fig 1). At the base of the heart there is a loud thrill and typical machinery murmur, particularly in the pulmonic area. The sound tracings are typical, though more intense, of a congenital cirroid aneurysm (Graph 1). There is an enlarged pulmonary conus, slight left ventricular hypertrophy. Clinically the patient is a well man. Should he be operated upon?

I cite this case to give Doctor Gross the chance to reemphasize the fact that a diagnosis alone of a patent ductus arteriosus does not warrant an operative procedure.

I wonder if many children who are diagnosed as having heart disease and later "outgrow it" do not really have some congenital defect as patent ductus arteriosus which closes spontaneously.

Finally, there are a few minor statements to which I must take exception. The "very tight" tying of the ligature about the ductus may lead to a rupture of the vascular coats and a subsequent fatal hemorrhage, gentle approximation of intimal surfaces would appear to me to be safer. I cannot subscribe to his belief that a persistence of a to-and-fro murmur means leakage through the wrinkled spaces of a collapsed ductus. It would appear to me that the operation for ductus arteriosus is ideal for the employment of silk ligatures and sutures throughout the procedure. I believe it would lessen the incidence of pleuritic effusions.

These minor disagreements must in no sense be construed to detract from my great admiration of this splendid piece of work.

DR ELLIOTT C CUTLER (Boston) It is a privilege to congratulate Doctor Gross on this piece of work as well as to congratulate the Association that a new furrow in the field of cardiac surgery has now been plowed. There are those, I have heard, who think I played a rôle in this work, and I should like to disabuse their minds of that. It is possible that Doctor Gross, since he has been with us a long time, may have known that I did contemplate, in the years when I was active in a new field in cardiac surgery, playing with the idea that the patent ductus might be ligated. But I saw an old man of 72 years of age with a loud machinery murmur and carefully studied him physiologically for some months, and decided that people who had patent ductus might live to adult life and that surgery was unnecessary.

As further evidence of my early interest in this matter is the fact that the first slide shown by Doctor Gross represented the situation in a child I studied in Cleveland and even contemplated operating upon.

Whatever credit there is in this work belongs entirely to Doctor Gross.

It is proper to point out, I think, since we are all interested in the education and training of competent surgeons, the backgrounds which give rise to this form of work, the form of work which your President in his masterful

presentation to the Society this morning pointed out as the type of work which the organizations of learned surgical groups should foster and encourage. This piece of work, as I look upon it, would not have come out unless Dr W E Ladd, of the Children's Hospital, and I had sort of a joint show where we share the same interns and have a joint service that provides for the young man adequate surgical training in children's surgery as well as in adult surgery. Moreover, this work might not have been accomplished, unless in the pediatric service of the Children's Hospital in Boston there had not been competent, wide-awake and courageous young pediatricians, because the surgeon alone, when he enters such a field, must have compatriots to help him. Moreover, it could not have occurred unless he had had at hand a fully equipped surgical laboratory, because one dares not enter into new fields where there are no signposts unless one can gain experience first upon animals. And, naturally, and finally, there must be some kind person to provide the patients.

This type of forward work in surgery represents the things that come from centers where there can be, for the growing young surgeon, all facilities—the laboratory, the intelligent and courageous colleagues in his medical service, and the patients to work upon. Moreover, such a work gives a tremendous stimulus to a great group of people.

The roentgenologist now is stimulated to make the diagnosis by a more competent study of the pulmonic conus. The pediatrician is stimulated to find patients who can be saved, and the surgeon, and the anesthetist, too, are studying better what is the best approach and what is the best anesthetic.

Doctor Gross, I hope, will elaborate upon reasons why the operation is desirable. In my time I had no knowledge of the fact that the majority of children born with patent ductus either die young or succumb early to cardiac failure or endocarditis. I believe he can give us statistical data revealing the natural mortality in this group, a mortality which in view of his experience might be, by surgical means, greatly lowered.

DR DAVID CHEEVER (Boston) I cannot refrain from adding my congratulations to Doctor Gross for his accomplishment of this remarkable surgical feat, and also to the Association for becoming the vehicle of its transmission to the surgical world.

I want to point out something that is a favorite viewpoint of many of us, all of us, in fact, and that is the transcendent importance of the basic sciences in the performance of such a thing as this—physiology and anatomy.

You noticed how Doctor Gross brought out the essential points in the topographic anatomy, which enabled him to accomplish this procedure with so much safety and precision. Now I admit, of course, that ligation of a patent ductus arteriosus is not likely to be an emergency procedure, so I imagine that anybody would have ample opportunity to look up his anatomy before performing it. I do not believe that Doctor Gross would feel obliged to do that, as a matter of fact, because, of course, it was the good fortune of the Harvard Medical School, where anatomy is still considered important, to be his alma mater.

DR ROBERT E GROSS In answer to Doctor Reid, I do not believe that the best way to obliterate the patent ductus has been found. I think it is a poor surgical procedure to ligate a vessel in continuity. However, in a small place between the great vessels in the mediastinum where space is at a premium, it appears to be impossible to doubly tie and divide the ductus. I had hoped to do it in one case in which the ductus was a little longer than in the other instances, but it appeared to carry with it too much danger.

Double ligatures have been used on the last two cases. It would probably

be a better procedure to doubly ligate, put the ligatures as far apart as possible, and to inject between them some sort of sclerosing fluid so that the intima would be destroyed and the vessel become thrombosed.

It is difficult to estimate the prognosis in individuals with a patent ductus arteriosus, because people who die of this lesion are apt to be reported, whereas others who go through life without any complications are rarely reported in the literature. The only statistics we have available at present are those of Maude Abbott, who collected, among her congenital cardiac cases, 92 individuals who had a patent ductus arteriosus without other lesion. About one-quarter of these lived to an elderly life, without any important complications. About one-quarter of them died of subacute bacterial endarteritis, and almost half of them died of cardiac failure.

I do not believe that all individuals in whom the diagnosis is certain should be operated upon. I think they should be followed for a number of years, because, as Doctor Reid has pointed out, there are individuals who will close off the ductus later in life or who will compensate for a small shunt. I have in mind several youngsters I have seen in the outpatient department who, as we have followed them through a period of years, show a heart which is slowing down, and which is not enlarged, they have no signs of cardiac failure, and they are developing normally in their physical stature. I think this type of individual should be left alone, because he may eventually close off his ductus, and the danger of letting him go untreated is less than the danger of operative intervention.

Regarding the age at which these people die, in Maude Abbott's series of 92 cases, the average age at death was 24 years.

Regarding advisability of operation in some of the cases that Doctor Reid mentioned, it is hard to tell an individual who is getting along fairly well that operation may be an advisable procedure. In the first case that we considered operating upon we ourselves thought the dangers of operation would be too great, and operation was deferred. However, the child was back in the hospital within a few months and died of subacute bacterial endarteritis. Thus, the fact that a patient has lived to 33 years, or one is 18 years of age without any particular trouble, is no indication that such an individual is going through the remainder of life without difficulty.

Regarding Doctor Reid's patient 18 years of age, who does not have endocardial infection, it is possible that such a patient may return later with subacute bacterial endarteritis. I say this because in the last few months I have been consulted in regard to three patients who had lived into the third decade without any evidence of cardiac disability, and all of them now have a fatal bacterial endocarditis.

I originally held the impression that patients who have subacute bacterial endarteritis should not be operated upon, because I felt that the manipulations in the region obviously would dislodge some of these vegetations and produce emboli. But since then, I have come to believe that some individuals with supervening subacute bacterial endarteritis should possibly be explored. I am not quite sure of this stand as yet, but it is possible that if you can close off the shunt you may stop the swirling of blood and the growth of the vegetations. Then, sulfapyridine or sulfanilamide would have a better chance to destroy those bacteria which are present.

A REVALUATION OF THE TREATMENT OF HEAD INJURIES*

JEFFERSON BROWDER, M D ,

AND

RUSSELL MEYERS, M D

BROOKLYN, N Y

FROM THE DEPARTMENT OF NEUROSURGERY OF THE KINGS COUNTY HOSPITAL, BROOKLYN, N Y

DURING the past 40 years a few clinically useful syndromes have been delineated from among the ever-increasing numbers of craniocerebral injuries with which the surgeon is required to deal. Among the better understood entities of traumatic origin may be mentioned simple and compound depressed fractures of the skull and subdural and epidural hemorrhages. In direct accord with the comprehension of the pathology and the pathogenesis of these conditions rational and effective therapy has been devised, and the major surgical principles relative thereto are no longer matters of controversy. The morbid anatomic disturbances underlying these entities frequently represent only a part of the entire pathologic process that may be encountered in any given instance, multiple lesions being the rule rather than the exception. There remains a large number of patients with brain trauma presenting bizarre clinical pictures dependent upon diversified pathologic states, the precise interpretation of which still escapes us. Cases in this group show clinical evidence of a grave cerebral insult characterized by profound alterations in constitutional, neurologic, and psychologic states. The gross pathologic features observable at autopsy in fatal cases often include cerebral lacerations, surface contusions, subpial, subarachnoid, and diffuse intracerebral petechial hemorrhages and variform zones of edema. These obvious lesions are frequently regarded by surgeons and pathologists as an adequate explanation of the symptomatology, clinical course and consequent death of the patient. We consider such an interpretation as being distinctly open to controversy. Certain less obvious but none the less real factors of a pathophysiologic nature resulting from the trauma and loosely spoken of as fluid imbalance, intramolecular derangements, circulatory alterations and vegetative dysfunction almost invariably accompany the gross anatomic findings. Indeed these factors may and do exist in fatal cases without demonstrable lacerations, hemorrhagic extravasations or edema of the brain.

The deficiencies of our understanding of the pathogenesis and physiologic pathology represented in the group of cerebral insults referred to above and under consideration in this paper, appear to be responsible for the present day controversies regarding the treatment of patients so injured. The wide disparity of viewpoint among those of seemingly equal authority concerning the

* Read before the New York Surgical Society, November 23, 1938. Submitted for publication October 31, 1938.

treatment of patients with craniocerebral injuries has been indicated by direct reference in a previous paper¹ The opinions expressed by many of these authors seem to represent personal impressions empirically arrived at and based largely upon their clinical experience Until further controlled investigations shall replace concepts reached chiefly by inference, our understanding of these obscure cerebral dysfunctions will be retarded with the consequence that logical therapy will be delayed The dearth of proper investigation may be for the most part attributed to the readiness with which authors and clinicians resort to the apparently sufficient notion of "compression" as an explanation for the constitutional, neurologic, and psychologic alterations observed in patients with brain trauma This notion, in turn, is traceable to the misdirected application of findings derived from certain animal experiments to clinical material The inappropriateness of this adaptation becomes apparent when the materials and methods of experimental conditions are compared with the circumstances attending traumatic cerebral insults In the animal, the physiologic alterations in blood pressure, pulse rate, respiratory rate and intracranial pressure were produced by pressure applied to the external surface of a brain possessed of an intact vascular tree, whereas in the traumatized human brain the lesion producing the dysfunction is usually intracerebral and is commonly associated with focal or more generalized thromboses of arterioles and venules Thus it becomes evident that the concept of "compression" as an explanation of the altered physiologic state of the traumatized patient may be applied in relatively few instances When the insufficiency of this traditional interpretation is widely recognized, new approaches to the problem may be devised and may prove of value in the delineation of further clinical entities, their pathogenesis, diagnosis, prognosis and treatment

A study of the historic development of the treatment of brain trauma since the time of Duret² and von Bergmann³ reveals two dominant influences The first of these was the demonstration of the "four classical stages of brain compression" by Kocher⁴ and Cushing^{5 6 7} The second was the finding of Weed and his collaborators⁸ that increased intracranial tension may be influenced by changing the osmotic pressure of the blood through the agency of hyper- and hypotonic solutions

According to Kocher the following sequence of events dependent upon increasing intracranial compression is noted

(I) Stage of Accommodation When an expanding agent begins to encroach upon the intracranial contents, its earliest effect is to displace some of the cerebrospinal fluid from the cranial vault The cerebral venous bed is the first to suffer the effects of this compression because of its relatively low tension, and the capillary vessels are the next in order As yet, however, the induced intracranial changes exert no recordable response on the part of the systemic circulation Headache, focal signs, apathy, drowsiness and slight distention of the retinal vessels constitute the chief manifestations The immediate prognosis in this stage is good and calls for expectant treatment

(II) Stage of Early Manifest Symptoms When the effect of the increasing

intracranial tension is sufficient to expel blood from the capillaries, anoxemia of the vital bulbar centers reflexly elicits a slight rise in systemic blood pressure. The stimulation of the vagal centers under the same circumstances produces a retardation of the pulse rate and a bounding character of the systolic impulse. Venous congestion of the head is revealed by facial cyanosis and dilatation of the venules of the lids and retina. Headache increases and excitement, vertigo, restiveness, delirium and unnatural sleep supervene. Focal signs, if present, become exaggerated and the respiratory rate is slowed. The immediate prognosis for life in this stage remains good.

(III) Stage of Advanced Manifest Symptoms. As the compressing force increases, capillary anemia and arteriolar stasis become severe and the medul-

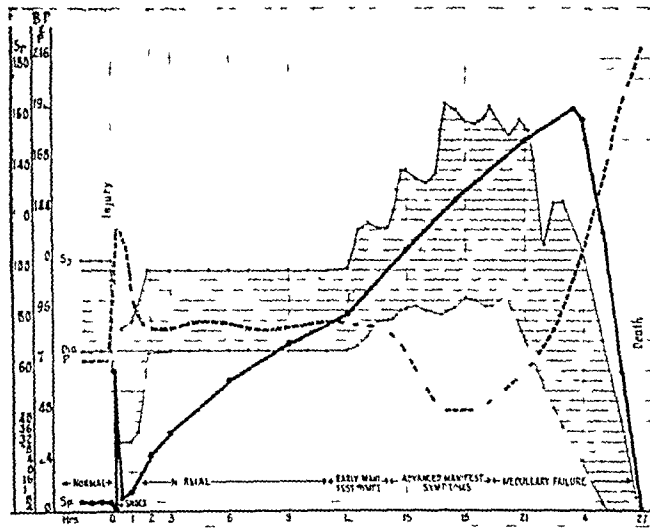


CHART 1—Illustrates the alterations in blood pressure and pulse rate following a rise in intracranial pressure according to the experimental findings in animals as noted by Kocher, Cushing and Cannon. After recovery from the initial shock, as the progressive increase in intracranial pressure is established, no change is imposed on the blood pressure and pulse rate until the intracranial pressure becomes equal to the diastolic and/or mean arterial pressure. When these levels are reached the blood pressure rises and the pulse rate falls. With increasing embarrassment, medullary failure appears and collapse becomes clinically evident. Sp = Systolic pressure, Ds = Diastolic pressure, P = Pulse, Sp = Cerebrospinal fluid pressure. (From Browder and Meyers. *Am J Surg*, 31, 3, 403-426, 1936.)

lary response produces a high blood pressure which is characterized by irregular fluctuations. The pulse takes on a typical vagal quality and its rate falls to 40 or 50 beats per minute. Cyanosis becomes extreme. The respirations are effortful, often characterized by periods of apnea or at times by Cheyne-Stokes cycles. The pupils may be disparate and may vary in size from time to time. The optic disks are choked. Reflexes are abolished. The mental state may range between deep coma and excitability. The prognosis in this stage is grave and immediate surgical intervention is required.

(IV) Stage of Medullary Collapse. As the intracranial pressure continues to increase, the overstimulation of the vital bulbar centers leads to their exhaustion. The blood pressure drops steadily, the pulse rate is accelerated, the cardiac rhythm becomes irregular and the heart action becomes poor. The

patient now presents the picture of shock. All reflexes are abolished. The pupils dilate and become fixed to light. Coma deepens and urinary incontinence occurs. Irregularities in the respiratory cycles are finally followed by respiratory failure. In this stage, prognosis is believed to be hopeless, regardless of the treatment employed.

Cushing, following the lead of Kocher, demonstrated experimentally in progressively increasing intracranial tension, the step-like rise of blood pressure which marks the period of medullary compensation. He⁵ proposed the following principle: "An increase of intracranial tension occasions a rise of blood pressure which tends to find a level slightly above that of the pressure exerted against the medulla." The schematic representation, Chart 1, com-

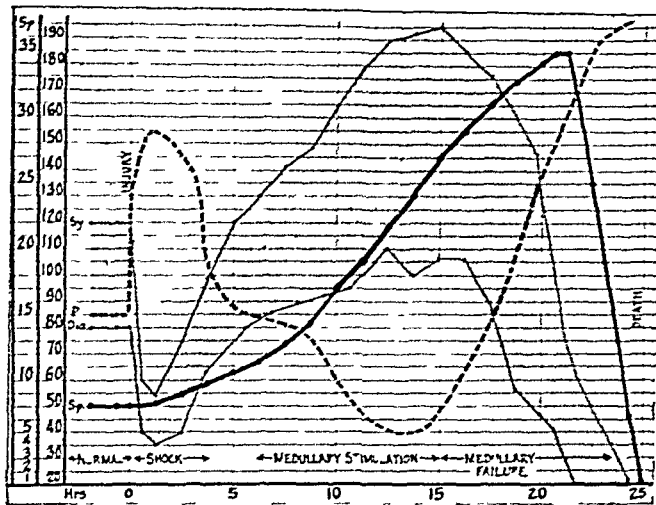


CHART 2—Illustrates the course of events following a rise in intracranial pressure according to a conception widely employed and taught in surgical practice. After recovery from the initial shock the intracranial pressure rises and there are a *pari passu* rise in the blood pressure and fall in pulse rate until medullary failure ensues. From this point on, the blood pressure falls, the pulse races and shock becomes evident leading almost inevitably to death. (From Browder and Meyers *Am J Surg*, 31:3 403-426, 1936.)

brates the findings of Cannon⁹ relative to the intracranial change immediately consequent upon trauma and the changes observed by Cushing⁶ under the experimental circumstances of increasing intracranial tension. Cushing later expressed the conviction that the data so acquired are clinically applicable and have their parallel in the physiologic disturbances resulting from sudden brain insults in the human, such as may occur in certain cases of apoplexy and several types of cerebral trauma. To quote his⁷ conclusions regarding this point: "Varying degrees of rapid increase in intracranial tension produce corresponding disturbances in the intracranial circulation. To these circulatory disturbances the symptoms of compression are solely due. The condition known as acute cerebral compression may be conveniently subdivided into four stages dependent upon the degree of circulatory alteration which has been reached. Each of the stages has its own more or less characteristic symptom-complex."

"The major or underlying symptoms originate in the centers situated in the

medulla and are only called out when the degree of intracranial tension begins to approach the arterial tension so that anemia is threatened. A circulatory condition in the medulla which borders upon anemia has the effect of stimulating the vasomotor center. Thus a rise in blood pressure is occasioned which restores the local circulation. The extent of this rise may be taken as an indication of the degree of advancement of the compression. Beyond a certain point, however, this reaction cannot take place. The vasomotor center under these circumstances fails and the respiratory efforts cease entirely.

"In conjunction with other symptoms a progressive increase in arterial pressure of a high degree of the same which has already been reached, or

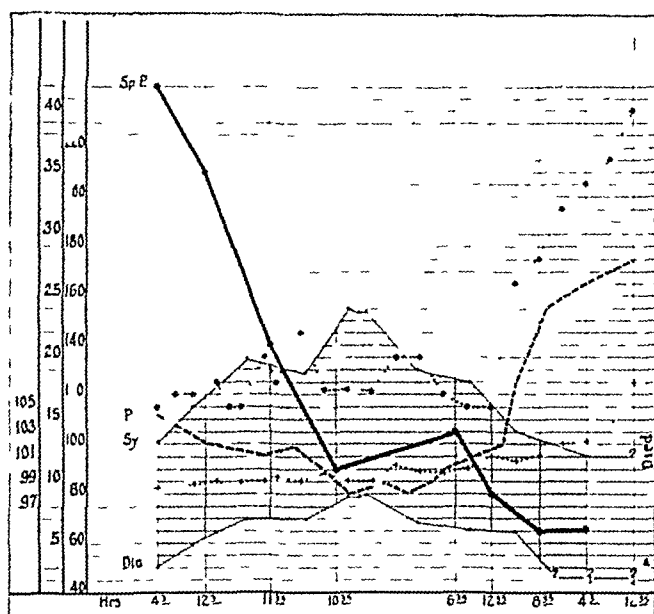


CHART 3—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate, respiratory rate and blood pressure in a patient, age 24, having a fracture of the skull and a clinically unrecognized epidural hemorrhage. The course of events during a 72 hour period, beginning within an hour of injury and ending at death, is recorded. A lack of conformance to the theoretically expected pattern is evident. Sp P=Cerebrospinal fluid pressure, R=Respirations, P=Pulse, T=Temperature, Sy=Systolic pressure, Dia=Diastolic pressure. (From Browder and Meyers. *Am J Surg*, 31, 3, 403-426, 1936.)

a pressure which exhibits, from moment to moment, great alterations in level may be taken as a certain indication of the advisability of early operative intervention. The intracranial tension should be relieved by the elevation of a large osteoplastic flap from one hemisphere or the other with a corresponding opening in the dura." Following this dictum, the treatment of cerebral injury was generally posited on the idea that cerebral compression is the prime factor in the production of the clinical picture. The decompression operation, therefore, was widely practiced in the treatment of brain trauma and in certain clinics to-day this surgical procedure is a commonly employed therapeutic measure. It is to be noted that in none of the human cases submitted by Cushing in substantiation of his conclusions did there appear any records of the mensuration of the cerebrospinal fluid pressure or of other methods of determining the intracranial tension.

Gradually there evolved in surgical teachings a clinical adaptation of the experimentally acquired idea, namely, that the observed alterations of blood pressure and pulse rate in an instance of brain trauma constitute a reliable index of the magnitude of intracranial tension and, therefore, of the indication for treatment (Pearce Bailey¹⁰ and Janeway¹¹) The basic features of this modification are graphically recorded in Chart 2 While the deductions from animal experiments possess at least the virtue of holding true for the

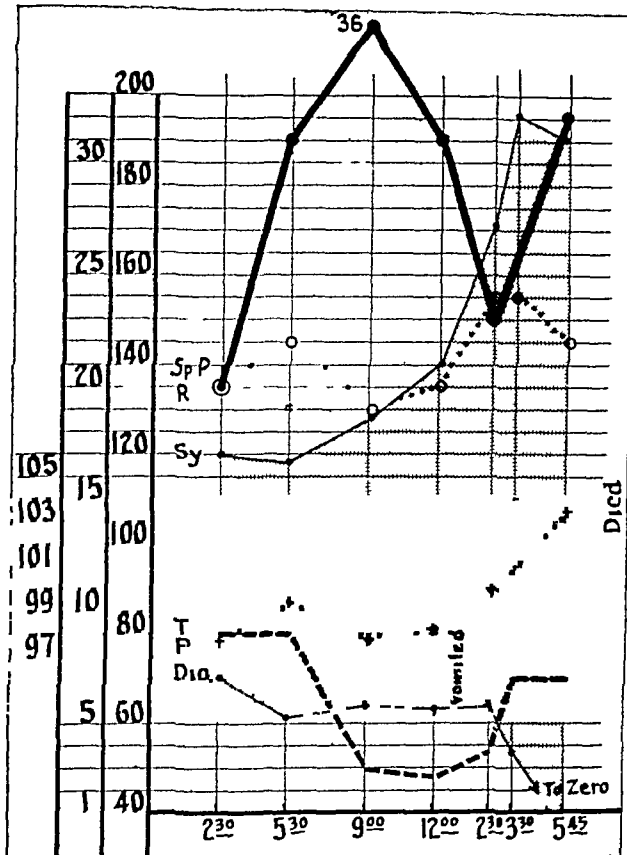


CHART 4—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate and blood pressure in a patient age 39, having a fracture of the skull and cerebral lacerations subdural and subpial hemorrhages, multiple petechial hemorrhages and diffuse cerebral edema. The course of events during a 15 hour period, beginning within an hour of injury and ending at death is recorded. As in Chart 3, a lack of conformance to the classical pattern is evident (From Browder and Meyers Am J Surg, 31, 3, 403-426, 1936)

conditions of the experiment, there is nothing from experimental sources and little from clinical data to substantiate the teachings as represented in Chart 2

The inability of the present writers to interpret clinically the altered brain functions of many traumatic cases in terms of the classical teachings led to a systematic study¹ of the behavior of the blood pressure, pulse, respirations, state of consciousness and cerebrospinal fluid pressure following craniocerebral injury. It was concluded from these investigations that measurable increased intracranial tension is rarely capable of producing medullary paralysis in cases of fatal head injuries. The classical pattern of signs consisting of

a steady rise above normal levels of systemic blood pressure, concomitant fall in pulse rate, decrease in respiratory rate, stupor, vomiting, *etc*, which has been alleged to indicate that the intracranial pressure is on the increase was not observed in this series of patients with brain insults. The conviction was, therefore, expressed that whether singly or in combination, the blood pressure, pulse rate, respiratory rate and the state of consciousness cannot be reliably regarded as an index of intracranial tension. Furthermore, repeated mensuration of the cerebrospinal fluid pressure cannot be made a criterion of the clinical state of the patient, his likely future course and the indication for therapy. Charts 3, 4, and 5 are examples of records of the

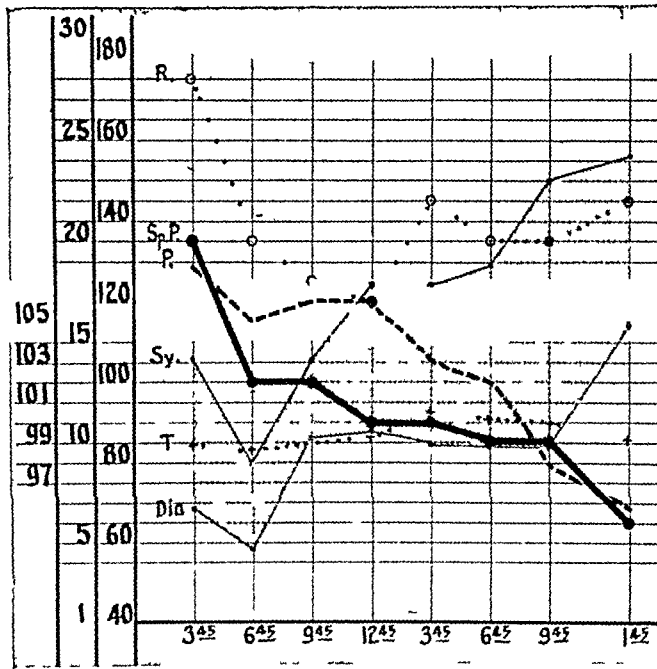


CHART 5—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate, respiratory rate and blood pressure in a patient, age 28, having a fracture of the skull and probably diffuse intracerebral hemorrhages and edema. The course of events during a 22 hour period, beginning within an hour of injury, is recorded. Rapid recovery ensued. Again, as in Charts 3 and 4, there is noted a wide departure from the schema usually taught. (From Browder and Meyers, *Am J Surg*, 31, 3, 403-426, 1936)

original 23 studies in these series. It may readily be seen that the bizarre patterns illustrated by these charts are irreconcilable with the classic Kocher schema. In fact, in clinical practice one rarely encounters a measured intracranial pressure which even remotely approaches the magnitude of that demonstrated by animal experiment to be necessary (80-100 Mm Hg) to alter the blood pressure and pulse rate. It is of further interest that in some of our earlier experiences, patients were encountered with stupor, elevated blood pressure, slow pulse rate and other manifestations which, according to the usual teaching, would have presaged the existence of a high degree of intracranial tension, in whom at operation the brain was found to be as much as 1 to 2 cm below the dural surface of the skull.

In order to properly evaluate the constitutional and neurologic manifes-

tations arising from increasing intracranial pressure in the human, under circumstances comparable to those obtaining in the animal experiments referred to above, a group of patients with large cranial defects was studied and the results reported in a previous communication¹² Under the condi-

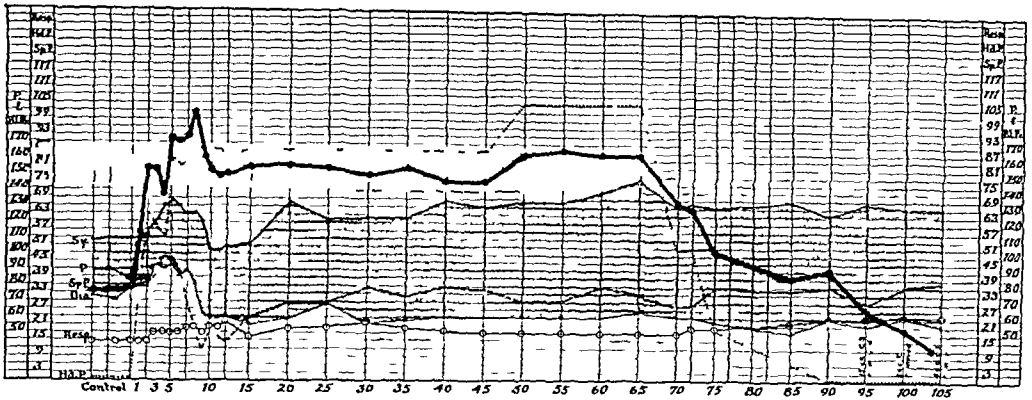


CHART 6—Illustrates the relationship of cerebrospinal fluid pressure pulse rate and blood pressure in a patient, age 52, who had undergone a partial extirpation of a left frontotemporal glioblastoma multiforme one and one half months before. Through the resulting skull defect the intracranial pressure could be readily altered. Although an intracranial tension well above that usually encountered clinically, was sustained for 90 minutes, the expected alteration of blood pressure and pulse rate was not encountered. Hd P=Head pressure, Sy=Systolic pressure, Dia=Diastolic pressure, P=Pulse, Sp P=Cerebrospinal fluid pressure, Resp=Respirations (Arch Surg, 36, 14, 1938)

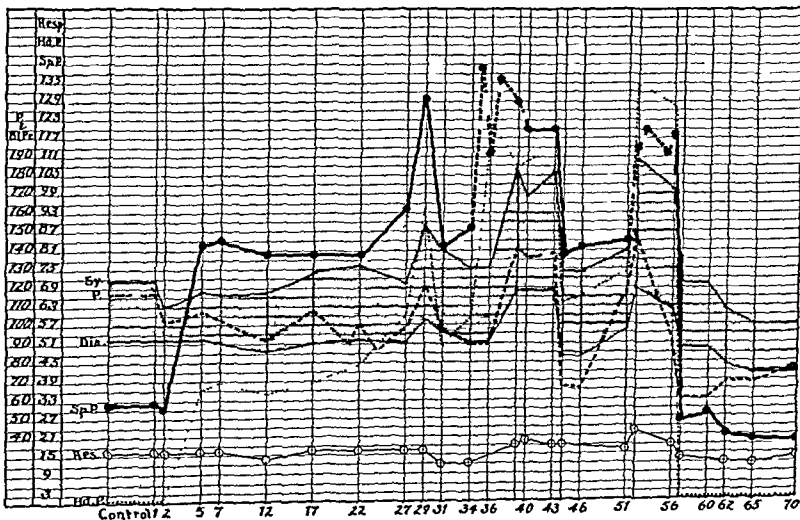


CHART 7—Illustrates the relationship of cerebrospinal fluid pressure pulse rate and blood pressure in a patient, age 39, who had undergone a subtotal extirpation of a right parietooccipital glioblastoma multiforme three months before. Through the resulting skull defect, the intracranial pressure could be readily altered. Although an intracranial tension, well above that usually encountered clinically, was maintained in the early part of the experiment, neither arterial hypertension nor bradycardia appeared. Only when the intracranial tension exceeded, in millimeters of mercury, that of the diastolic and/or mean arterial pressures were significant systemic changes produced, and even these were not strictly according to the expected pattern since the pulse rate changes followed, rather than ran counter to, those of the blood pressure (Arch Surg, 36, 15, 1938)

tions of this experimental set-up the intracranial pressure could be altered within limits to any desired extent by applying pressure over the cranial defect, and the resulting changes of the blood pressure, pulse rate, respiratory rate and state of consciousness recorded. A review of the records of 13 such

experiments led to the conclusion that no clinically significant alterations in blood pressure, pulse rate, respiration and mental state were produced by advancing the intracranial tension until this pressure reached or exceeded the level of the diastolic blood pressure. In general, support was lent to the observations derived from the animal experiments of Duret,² Kocher,⁴ Cushing^{5, 6, 7} and others. However, attention should again be directed to the fact that intracranial tensions of a magnitude sufficient to produce alterations in blood pressure, pulse rate, *etc.*, are far in excess of those clinically encountered. Charts 6 and 7 are graphic representations of the observations made in two of the human experiments in this series. The important implication arising from these experiments is that, in a consideration of altered constitutional and psychologic states in a patient with brain trauma, it becomes necessary to postulate factors other than increased intracranial tension to explain such changes.

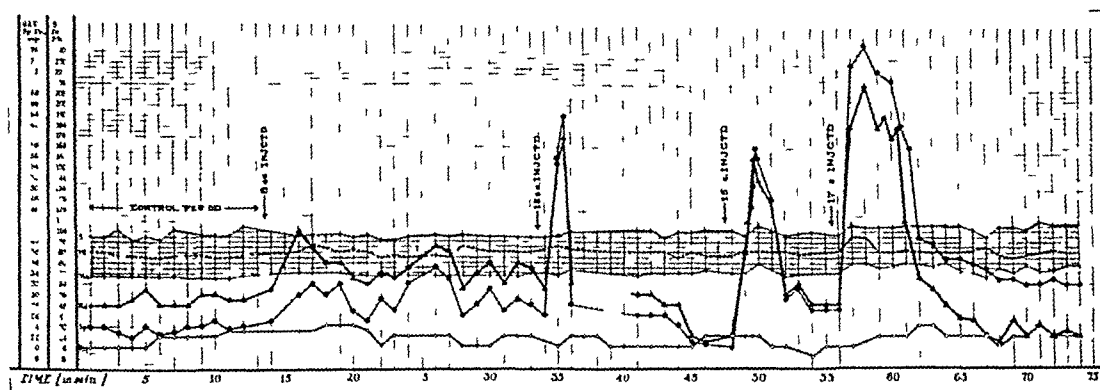


CHART 8—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate and blood pressure in a patient, age 19 who had a midline cerebellar astrocytoma. A needle was passed into the right lateral ventricle, and through this, physiologic saline was injected so as to alter the intracranial tension. It may be seen that the vital signs were not appreciably altered by acute elevations of the intracranial pressure to levels well above those usually recorded clinically. Sy = Systolic pressure, Dia = Diastolic pressure, P R = Pulse rate, Hd = Intraventricular pressure, Sp P = Cerebrospinal fluid pressure, Resp = Respiration.

The information obtained from both clinical and experimental investigations in man, relative to the factor of intracranial tension, appears to place this agent in a rôle of small significance, at least with reference to its utility in accounting for the altered vital signs associated with severe trauma of the brain. Nevertheless the question arose as to whether pressure exerted from within the ventricular system might not prove adequate to alter the blood pressure, pulse rate, respiration and mental state at a magnitude considerably less than that found necessary to effect such changes when applied to the external surface of the brain. Therefore a method* was devised whereby the intraventricular pressure could be directly altered and the effect on the

* With the patient lying in the lateral position, a ventricular needle was introduced into the lateral ventricle and secured in place by a special device designed to prevent the escape of cerebrospinal fluid. Through this needle saline solution could be injected under controlled pressure. The experimental set-up was such that at intervals the blood pressure, pulse rate, respiratory rate, cerebrospinal fluid pressure and intraventricular pressure could be recorded.

vital signs of an increase in tension could be recorded. In a series of five such experiments the results obtained were essentially consistent with those observed following the application of an external pressure agent. Charts 8 and 9 are graphic illustrations of the results obtained under these conditions. These findings appear to warrant the exclusion of increased intraventricular pressure as an adequate explanation for the observed clinical alterations of vital signs in patients with brain trauma.

These three lines of evidence concerning the factor of cerebral compression—that derived from observations on the behavior of the systemic blood

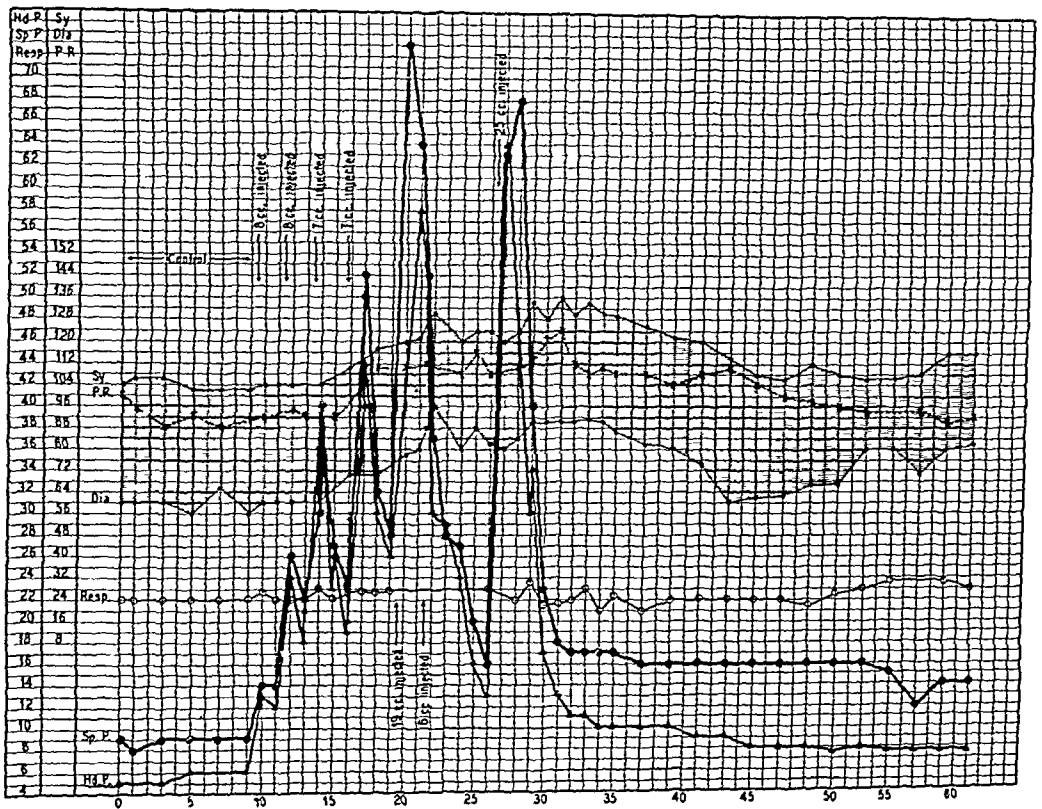


CHART 9—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate and blood pressure in a patient, age 32 with a well established hysteria characterized by mutism. A needle was passed into the right lateral ventricle, and through this physiologic saline solution was injected so as to alter the intracranial tension. As in Chart 8, the changes in the vital signs that were produced by the marked acute elevations of intracranial tension were clinically insignificant and in any case were not those of the classically expected pattern. Sy = Systolic pressure, Dia = Diastolic pressure, P R = Pulse rate, Resp = Respirations, Sp P = Cerebrospinal fluid pressure, Hd P = Intraventricular pressure.

pressure, pulse and spinal fluid pressure following craniocerebral injury, that from the alterations in vital signs associated with changes in intracranial tension experimentally produced by an external pressure agent, and that from the alterations in vital signs associated with changes in intracranial tension experimentally produced by the application of an intraventricular pressure agent—lend strong support to the view already expressed, namely, that the changes in the constitutional, neurologic and psychologic states of patients showing evidence of severe trauma of the brain, are not applicable in terms of increased intracranial tension *per se*. The indication for decompression procedures would appear to be rare in the light of the foregoing, and in point

of fact, this same conclusion has been empirically reached on clinical grounds. This contention may be held to apply with equal force to repeated drainage of cerebrospinal fluid by lumbar puncture when this has as its primary goal the reduction of intracranial pressure. This does not mean to imply that patients are never encountered in whom the reduction of even a mildly increased intracranial tension may not favorably influence the vital signs for a short period. In such cases, however, our interpretation has been that the less obvious factors consequent upon craniocerebral violence ("intracellular edema," "fluid imbalance," "intramolecular derangements," *etc*) are present and probably are the prime determinants of the altered vital signs. That such lesions may in turn be further changed by mechanical factors producing increased intracranial tension is reserved as a definite and plausible probability. Examples of this kind, however, are few.

If, then, the treatment of the majority of patients with severe brain injuries is not to be directed at the mere reduction of intracranial tension, it must of necessity be concerned with an attempt to improve the function of the damaged intracerebral tissues by other means. There are several meritorious contributions dealing with the histopathology of cerebral tissues altered by trauma^{13, 14, 15}. However, in the present state of our knowledge, little of a precise nature is known concerning the correlation between these lesions and the dysfunction produced thereby. Much less information is available regarding the underlying biochemical and biophysical cellular changes. Whether the effects of the trauma are imposed directly on the parenchyma of the brain or whether the changes are secondary to humoral (blood and cerebrospinal fluid) alteration, cannot be stated. Here is a field sorely in need of careful investigation.

In the historic development of the treatment of brain trauma, the contribution of Weed and McKibben,⁸ which appeared in 1919, stands as the second dominant influence. These workers demonstrated, in a series of well controlled experiments, that the intracranial pressure could be reduced in the normal animal by the intravenous injection of hypertonic solutions. Clinicians were prompt in recognizing the applicability of this finding to therapeutics and employed it widely in the management of a variety of intracranial lesions. The early optimism attending the use of these solutions (dextrose and sodium chloride) was somewhat tempered by the experience that an occasional patient treated in this manner showed an immediate untoward reaction. Accordingly, in 1929, one of us (Browder¹⁶) carried out observations of the sequence of physiologic events following the intravenous administration of a 100 cc dose of 50 per cent dextrose solution. In a series of five patients, all of whom presented clinical evidence of recent brain trauma, there was disclosed, following the injection, the expected initial reduction in cerebrospinal fluid pressure, but within the course of one and one-half hours there ensued a secondary rise to a level approximately 4 Mm Hg higher than that initially recorded. In a second group consisting of three patients also with recent brain trauma, the immediate response to the injection of this dose of hypertonic dextrose

solution was a rise in the cerebrospinal fluid pressure of approximately 8 Mm Hg. At no time during the period of observation following the injection was there noted a fall of pressure below that of the control period. A third type of reaction was that observed in a severely injured patient in whom there occurred, almost immediately after the administration of the dextrose solution, an abrupt rise of the systolic and diastolic blood pressure and a concomitant rise in the cerebrospinal fluid pressure from the control level of 28 Mm Hg to a maximum of 66 Mm Hg within a 15 minute period. Attending these changes the respiration became accelerated and labored, the pulse rate rose

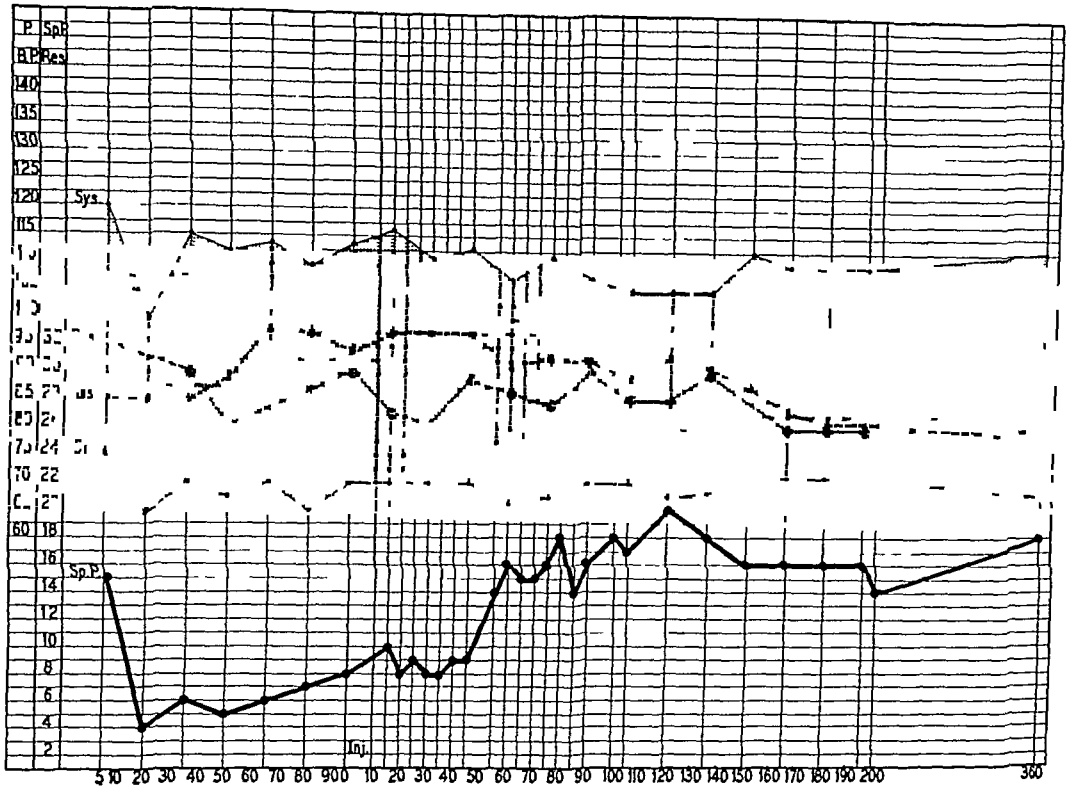


CHART 10.—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate and blood pressure in a patient, age 28, with a severe craniocerebral trauma. Nine hours after injury 100 cc of 50 per cent solution of dextrose were injected intravenously. The fall of cerebrospinal fluid from 15 Mm Hg to 4 Mm Hg following the introduction of the needle could not be explained. As recorded, there was a rise in cerebrospinal fluid pressure subsequent to the injections. The independent readings at 360 minutes after the injections were made two hours before a second administration of a similar amount of dextrose, the effects of which are recorded in Chart 11.

to an extreme level, cyanosis appeared and the patient died one hour and 50 minutes following the injection. This latter experiment dramatically demonstrated that the use of hypertonic dextrose solution in the routine treatment of patients with recently inflicted brain trauma is not without danger. In 1932, Jackson,¹⁷ on the basis of findings derived from similar experiments, arrived at the same conclusions. Consequently, hypertonic solutions were employed by us with much reserve during the first 48 to 72 hours following injury. Between 1930 and 1936, many clinical observations were made following the use of hypertonic solutions, and the unpredictable reactions observed indicated that our understanding of the physiologic actions of these

HEAD INJURIES

solutions was wanting. Therefore, in 1936, experiments, similar in principle but more elaborate than those initially conducted, were resumed by Dr. Floyd Bragdon, then Resident Neurosurgeon at the Kings County Hospital. Thus far, detailed observations of the effects of various hypertonic solutions on the intracranial tension as measured by the cerebrospinal fluid pressure have been recorded in 52 experiments. The solutions used in these experiments include sodium chloride, dextrose, sucrose and the new pharmaceutical prepa-

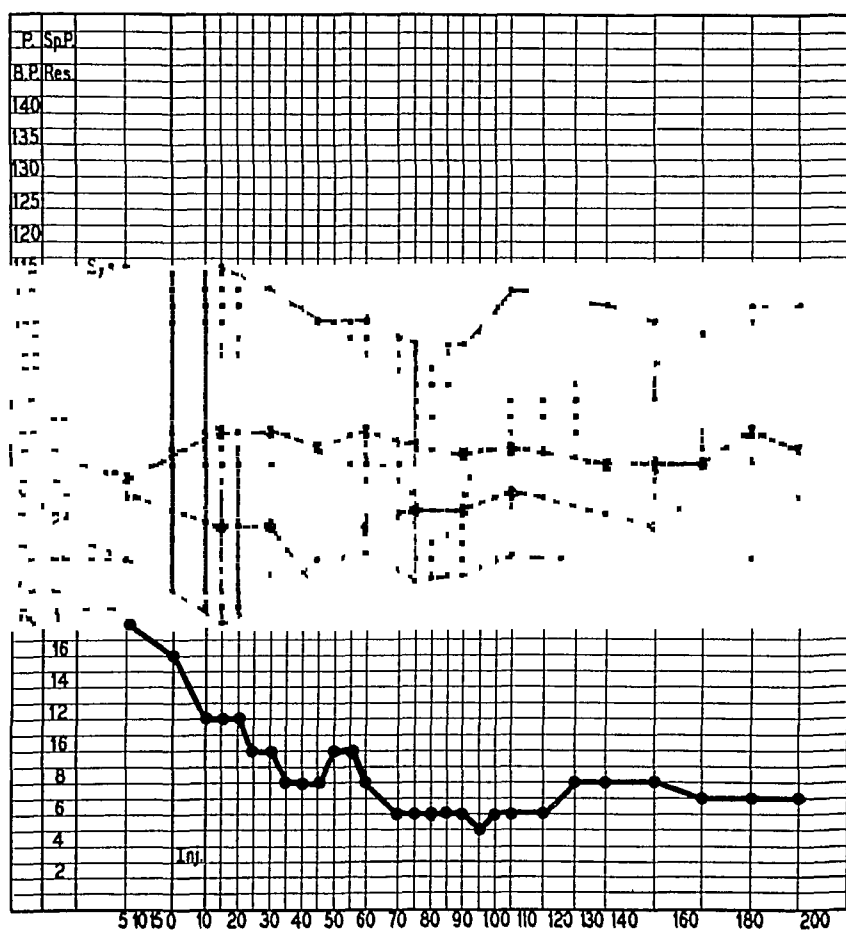


CHART 11—Illustrates the relationship of cerebrospinal fluid pressure, pulse rate and blood pressure in the same patient referred to in Chart 10. Here, by contrast with its earlier rise, the cerebrospinal fluid pressure was reduced following the intravenous injection of an hypertonic solution. The capricious character of response is to be emphasized.

ration, sorbitol. It may be stated, on the basis of these investigations, that in the normal human as in the animal experiments of Weed,⁸ the hypertonic solutions usually effect a reduction in cerebrospinal fluid pressure when administered intravenously. In contrast to this action, it was noted that following the administration of these solutions to patients with clinical evidence of brain trauma, the physiologic effect on the cerebrospinal fluid pressure could not be predicted. Charts 10 and 11 graphically illustrate the capricious character of the effects recorded following two successive intravenous injections of dextrose in one such patient. There is no well substantiated explanation for these irregularities.

On the basis of the data derived from the 1929 series of experiments, it

was proposed at that time that the interruption of the cerebrovascular channels by trauma establishes a physiologic disturbance so that hypertonic solutions frequently do not produce the expected effect. The more recent experiments of Doctor Bragdon have shown that these abnormal reactions may be encountered in a variety of cerebral lesions other than those due to trauma and that anatomic interruption of the vascular tree is not an essential prerequisite. In the light of this evidence it seems defensible to hold that the routine use of hypertonic solutions in the treatment of patients with brain trauma is not only ineffective in certain cases, but may actually produce untoward reactions. Under circumstances in which it seems desirable to utilize this form of treatment, it must be understood that the fall in cerebrospinal fluid pressure, if it occurs at all, is seldom sustained at the reduced level for a period of more than one and one-half to two hours and that undesirable effects may on occasion follow its use.

A review of the several lines of evidence thus far presented leads again to a recognition of the point to which reference has already been made, namely, that the development of rational methods of treatment for that group of patients which represents the object of our present inquiries awaits a more precise understanding of the pathologic physiology underlying intracerebral trauma. To-day, as formerly, the treatment of the majority of patients with severe brain damage, exclusive of those with depressed fractures of the skull, epidural and subdural hematoma and large intracerebral clots, remains highly empiric. Therefore, when the surgeon encounters a clinical problem in craniocerebral trauma his first responsibility is to determine with reasonable certainty whether there is present one or more of these four operatively amenable lesions associated with the more generalized trauma of the brain. Inasmuch as reliable differential diagnosis is commonly not possible on the basis of clinical findings alone, methods of greater precision become necessary. It has been quite generally accepted that routine roentgenologic examination of the skull be employed in order to establish the position of the falx cerebri and pineal body. It has been our experience that while this measure may aid in determining the presence of an intracranial blood clot of surgical significance, it is incapable of indicating the location of the lesion with exactness. Furthermore, we have occasionally met cases in which, paradoxically enough, the falx occupied a midline position and in which a sizable intracranial hematoma was proven to exist. In addition, it is to be recognized that calcific deposits upon which the roentgenographic demonstration of the pineal body depends are rarely present in young individuals and are absent in a fair percentage of adults.

Accordingly, in relatively fresh cases demanding prompt and precise diagnosis as a basis for therapy, we have resorted to aerographic roentgenologic studies of the head. One of two methods is open to us here. The introduction of 40 to 60 cc. of air as contrast medium into the subarachnoid space of the lumbar thecal sac (encephalography), or the introduction of air directly into the ventricular system in quantities sufficient to obtain complete

filling (ventriculography) Our experience during the past five years has established the usefulness of this method of examination, indeed, its indispensability in the management of certain instances of severe brain injuries

When the diagnostic issue, in a given case, has been resolved to the exclusion of the surgically amenable lesions by the application of one or a combination of the above methods, the management of craniocerebral trauma reduces itself to palliative, supportive and hygienic measures These include the following

(1) A position in bed which permits an unobstructed return of venous blood from the head and a free respiratory exchange these requirements are usually best met in a moderate Fowler's position with the patient turned on the side in such a posture as to permit the tongue to gravitate forward and to give free drainage of mouth and nasal secretions Careful turning from side to side, in log fashion, at periodic intervals will aid in the prevention of hypostatic congestion

(2) Sufficient sedation to insure against excessive motor activity chloral hydrate bromides, paraldehyde and the barbiturates have proven useful for this purpose

(3) Mechanical restraint to prevent further injury there are several methods of restraining a patient, all of which possess merit provided certain precautions are exercised A crib type of bed is an indispensable necessity When applying restraints in the form of camisoles, twisted sheets, cuffs and other devices which immediately contact the body, particular care should be taken that no undue traction is exerted against the axilla lest the nerve trunk coursing from the brachial plexus be damaged Bony prominences should be padded to prevent the occurrence of cutaneous abrasions

(4) The control of body temperature this important item calls for the simultaneous recording of both axillary and rectal temperatures at two hour intervals during the first 36 hours following the injury In the event that the rectal temperature rises above 102° F, brisk rubbing of the skin with warm wet cloths followed by fanning is to be instituted and continued until the temperature falls below this critical level If the temperature cannot be controlled by these measures, colonic instillation of cold tap water in quantities of one to two liters may be resorted to Each instillation of cold tap water should be left in the colon for five to seven minutes after which it is to be drained away and replaced This may be repeated until the desired reduction of temperature is attained The axillary temperature should be recorded every ten minutes during this procedure and ought not to be reduced below 100° F Too rapid a reduction of temperature is to be avoided, and the appearance of cyanosis is a signal for the temporary interruption of the treatment Under exceptional circumstances it may be necessary to resort to wet packs The point to be given emphasis is that temperatures are more readily controlled at lower levels than when they exceed 104° F

(5) The maintenance of an adequate water balance and of the patient's nutrition the early passage of a Levine tube through the nose in nonresponsive

patients serves several purposes. Through it magnesium sulphate in three ounce doses may be introduced. The dehydrating action of this purgative may have a beneficial cerebral effect and in any event the purgation produced may aid in cleansing the gastro-intestinal tract of noxious substances. A body fluid balance may be maintained by the administration of fluids and food through the tube thereby making repeated introduction of subcutaneous and intravenous fluids unnecessary. In general two liters in a 24 hour period is an average quantity, but the amount of fluid administered will of necessity be governed by the degree of febrile state prevailing. In any case an excessive dehydration is to be avoided. The length of time these measures are to be continued will naturally depend on the progress of the patient. On occasion they have been employed to a successful conclusion for as long a period as five weeks.

SUMMARY AND CONCLUSIONS

It may be held that the traditional account of the manifestations of cranio-cerebral trauma in terms of brain compression is incapable, in the majority of cases, of being reconciled with the data derived from clinical, pathologic and experimental investigation. Similarly, explanations attributing the observed changes to such gross lesions as lacerations, contusions, subarachnoid hemorrhages and edema fail, except in a few instances, to provide satisfying answers. The evidence available rather indicates the necessity of experimental inquiry into the nature of the more subtle pathologic intracerebral disturbances, particularly of the derangements of the physicochemical constitution of nerve cells and their processes. Until precise knowledge along such lines is acquired, bringing with it an understanding of the pathogenesis of the majority of severe cerebral injuries comparable to that at present possessed in connection with epidural, subdural and intracerebral hemorrhages and with depressed fractures of the vault, just so long will treatment remain empiric.

Since it has been demonstrated that increased intracranial tension is rarely the basic problem in cranio-cerebral trauma, it is evident that efforts to reduce it, by either surgical or chemical means, are largely misdirected. Furthermore, and this with particular reference to patients having severe degrees of brain damage, the indiscriminate use of hypertonic solutions may produce unexpected and untoward results.

The proper management of head injuries requires the clinician to determine whether or not there are present any of the following lesions: significantly depressed fractures of the vault and epidural, subdural and intracerebral hematoma. These alone may be benefited by surgical procedures. Other pathologic processes than these call for the institution of supportive measures and, inasmuch as they frequently complicate the operable type of lesion, similar treatment will in a majority of cases be required to supplement the surgical therapy. Differential diagnosis is often rendered difficult by virtue of the fact that generalized cerebral insults commonly coexist with the sur-

gically amenable conditions In such problems, cerebral aerography may help to clarify the diagnosis It has proven an almost indispensable agent in our hands and experience has shown that it may be carried out with reasonable safety even in recently injured patients

REFERENCES

- ¹ Browder, J, and Meyers, R Observations on Behavior of the Systemic Blood Pressure, Pulse and Spinal Fluid Pressure Following Craniocerebral Injury *Am J Surg*, 31, 403, 1936
- ² Duret, M H Recherches anatomiques sur la circulation de l'encephale *Arch de physiol norm et path*, 1, Ser 2, 60, 316, 664, 919, 1874
Duret, M H Notes sur la physiologie pathologique des traumatismes cerebraux *Gaz Méd de Paris*, vi, Ser 5, 599, 612, 624, 1877
Duret, M H Etudes experimentales et cliniques sur les traumatismes cérebraux *Publ du Progrès méd*, Paris, 1878
- ³ Von Bergmann, E Die Lehre von der Kopfverletzungen *Deutsch Chir*, 30, 2 Teil, 266, 341, Stuttgart, Enke, 1880
- ⁴ Kocher, T Hirnerschütterung, Hirndruck und chirurgische Eingriffe bei Hirnerkrankungen *Nothnagel's Specielle Pathologie und Therapie*, Bd 18, 3 Teil, 2 Abteilung, S 81, 1901
- ⁵ Cushing, H Concerning a Definite Regulatory Mechanism of the Vasomotor Centre Which Controls Blood Pressure During Cerebral Compression *Johns Hopkins Bull*, 12, 290, 1901
- ⁶ Cushing, H Some Experimental and Clinical Observations Concerning States of Increased Intracranial Tension *Am J Med Sci*, 124, 375, 1902
- ⁷ Cushing, H The Blood Pressure Reaction of Acute Cerebral Compression *Am J Med Sci*, 164, 1017, 1903
- ⁸ Weed, L H, and McKibben, P S Pressure Changes in Cerebrospinal Fluid Following Intravenous Injections of Various Concentrations *Am J Physiol*, 48, 512, 1919
Weed, L H, and Hughson, W Systemic Effect of Intravenous Injection of Solutions of Various Concentrations with Especial Reference to Cerebrospinal Fluid *Am J Physiol*, 58, 53, 1921
Weed, L H, and Hughson, W Intracranial Venous Pressure and Cerebrospinal Fluid Pressure as Affected by Intravenous Injection of Solutions of Various Concentrations *Am J Physiol*, 58, 101, 1921
- ⁹ Cannon, W B Cerebral Pressure Following Trauma *Am J Physiol*, 6, 91, 1901
- ¹⁰ Bailey, P Diseases of the Nervous System Resulting from Accident and Injury New York and London, D Appleton & Co, 44 ff, 1906
- ¹¹ Janeway, T C The Clinical Study of Blood Pressure New York, Appleton, 139 ff, 1904
- ¹² Browder, J, and Meyers, R Behavior of the Systemic Blood Pressure, Pulse Rate and Spinal Fluid Pressure Associated with Acute Changes in Intracranial Pressure Artificially Produced *Arch Surg*, 36, 1, 1938
- ¹³ Rand, C W, and Courville, C B Histologic Studies of Brain in Cases of Fatal Injury to the Head, Cytoarchitectonic Alterations *Arch Neurol and Psychiat*, 36, 1277, 1936
- ¹⁴ Courville, C B, and Kimball, I S Histologic Observations in Case of Old Gunshot Wound of the Brain *Arch Path*, 17, 10, 1934
- ¹⁵ Rand, C W, and Courville, C B Histologic Changes in Brain in Cases of Fatal Injury to the Head, Changes in Nerve Fibers *Arch Neurol and Psychiat*, 31, 527, 1934
- ¹⁶ Browder, J Dangers in the Use of Hypertonic Solutions in the Treatment of Brain Injuries *Am J Surg*, 6, 1213, 1930
- ¹⁷ Jackson, H, *et al* The Effect of Hypertonic Dextrose Solutions on Intracranial Pressure in Acute Cranial Injuries *Chi Surg Soc*, October 7, 1932

DISCUSSION — DR IRA COHEN (New York) said that Doctor Browder had shown by experimental evidence that which the modern trend of clinical experience has demonstrated, namely, that in the operative treatment of head injuries one must have a focal point of attack. In other words, the surgeon operates for depressed or compound fractures, for collections of blood above or below the dura, and, in rare instances, for a collection of blood in the cerebral substance. The trend nowadays has been away from decompressions for generalized decreased intracranial pressure. Bradycardia is not a true index, as such, of increased intracranial pressure. It is not always present when pressure is high, and all surgeons have seen patients after a head trauma who have had bradycardia for weeks without other evidence, either subjective or objective, of increased intracranial pressure. On the other hand, almost all know from their work in brain abscesses and brain tumors that increased cranial pressure, particularly in abscess cases, can and does show itself by bradycardia. Finally, measuring the pressure of the cerebrospinal fluid by spinal puncture is not always a true index of the intracranial pressure. Doctor Browder has had numerous occasions, as have all surgeons who operate upon brain tumors or deal with advanced papilledema, where, upon incising the dura, the brain tends to herniate, yet, in the pre-operative stage of such a patient, the intracranial spinal pressure was within normal limits. Doctor Cohen said that he had not had an opportunity to carry out all studies in acute traumatic cases, but regarded them of great value in some instances. Doctor Browder, he said, had found them of value either by direct injection into the ventricle or by endolumbar injection. Doctor Cohen felt that if he were to employ air, he would be inclined to inject it into the ventricle, as being the safer procedure. Moreover, inspection through the bur hole might of itself be of diagnostic value. Doctor Cohen said that he was a firm believer in, as a routine, at least a diagnostic puncture when the patient enters the hospital, particularly in mild cases of head trauma, for, all too frequently, in what seems to be a very mild trauma one finds evidence of subarachnoid bleeding. In spite of the fact that hypertonic solution sometimes gives a reverse reaction and raises the level of the spinal fluid pressure, there are times when its use is indicated in selected cases, though not as a routine. There should not be a routine in handling these cases at all because each is a law unto itself. Yet a restless patient, resistant to relatively large doses of sedatives, will often quiet down promptly after a lumbar, or after the use of an intravenous hypertonic solution. Doctor Browder's investigation is particularly important in that it shows that there is an as yet unexplained factor in head injuries, unexplained from the very start. What is back of the picture of concussion is not known, from there on right straight through to the case of the patient who dies following a head injury and in whom microscopic examination reveals no cause. Investigations such as Doctor Browder's enable one to separate the explained from the unexplained, with a view to some day understanding the unexplained factors.

DR JEFFERSON BROWDER (closing) — In answer to Doctor Berry's question regarding the use of morphine in the treatment of patients with craniocerebral injuries stated that there had been a general impression that morphine sulphate was a dangerous drug to give a patient during the acute phase of a head injury. Detailed observations concerning the alterations in cerebrospinal fluid pressure following subcutaneous injection of morphine (gr $\frac{1}{4}$) show a definite rise in the spinal fluid pressure. Similar studies carried out after the administration of luminal and avertin demonstrated a somewhat comparable rise in cerebrospinal fluid pressure. It seemed that any drug that had a

sedative effect, if given in moderately large doses, would probably raise the cerebrospinal fluid pressure

Doctor Blowder said that Doctor Goetsch justly raised the question of the usefulness of decompression operations in the treatment of brain trauma. Also whether patients with mild to moderate brain trauma may not present signs and symptoms dependent upon an excessive production of cerebrospinal fluid as contrasted with the more seriously injured ones who often showed no evidence of increased cerebrospinal fluid pressure. Subtemporal decompression was considered most effective where there was an accumulation of blood or cerebrospinal fluid in the subdural space. No doubt, there were instances of increased intracranial tension secondary to trauma that may be improved by this operation, however, the studies of Doctor Blowder and his coworkers during the past eight years indicated that "pressure," in some cases, may be considered a contributing factor but certainly not the primary issue. Whether or not there was an excess of cerebrospinal fluid in the mild to moderate degrees of head trauma could not be stated.

MASSIVE HEMORRHAGE IN PEPTIC ULCER

THE TRANSFUSION TEST FOR DETERMINING THE NECESSITY OF OPERATION

J WILLIAM HINTON, M D

NEW YORK, N Y

FROM THE FOURTH MEDICAL AND SURGICAL DIVISIONS OF BELLEVUE HOSPITAL, NEW YORK, N Y, DRs CHARLES H NAMMACK
AND CARL G BURDICK, DIRECTORS

THE active stage of a massive hemorrhage from a peptic ulcer occasionally confronts one with the necessity of deciding whether to operate as a life-saving measure. This decision as to operative intervention is most difficult in any case, and unfortunately the difficulty is enhanced by the varying conceptions of hospitals regarding cases included under the category of massive hemorrhage. Obviously, also, the indications for both medical and surgical treatment are inevitably variable. It is, therefore, worth remembering that the following conclusions are drawn from cases in a large municipal hospital with an active ambulance service. They would not necessarily have equal validity elsewhere.

The surgeon, during the past decade, has become ultraconservative in treating patients with massive hemorrhage from a peptic ulcer. As a result the gastro-enterologist has assumed greater responsibility in handling these cases—and his teaching is that a fatality from hemorrhage occurs, seldom, if ever. The surgeon with an active hospital service, however, who must handle some of the more desperate cases of massive hemorrhage, is aware that a certain percentage of these will prove fatal under any method of conservative management. In our experience, approximately 10 per cent of the patients with massive hemorrhage have died in spite of the conservative treatment. A consideration of this group, in which conservative measures fail, is the chief object of this paper.

The proportion of peptic ulcers in which massive hemorrhage results must be analyzed from the standpoint of patients who have been hospitalized and those under an ambulatory regimen. Thus, on the Fourth Medical and Surgical Divisions at Bellevue Hospital, with a 200 bed capacity, 90 patients with peptic ulcer were admitted yearly, of whom 12, or 13 per cent, were admitted for massive hemorrhage. On the other hand, a review of 570 cases of unoperated ulcers in our clinic, all under proper medical supervision, shows that only 3.3 per cent suffered from massive hemorrhage. The condition is evidently several times more frequently observed in the more seriously ill hospitalized patients.

During a 10-year period, from 1928 to 1937 inclusive, there were 135 cases of massive hemorrhage, with a mortality of 12, under conservative medical management. It is interesting to note that of this group six died

Submitted for publication October 10, 1938

without blood transfusions and six after one or more transfusions. It would seem, therefore, that a definite percentage of massive hemorrhages will prove fatal under either type of conservative management, *i e*, regardless of transfusions.

Another important factor, perhaps the most important factor, in the causation of massive hemorrhage is the location of the ulcer. It is the posterior duodenal ulcer that is most likely to prove fatal. In our 12 fatal cases of massive hemorrhage, we encountered gastric lesions of the lesser curvature in the pars media in only two instances, while the remaining ten were all cases of posterior duodenal ulcer with erosion through the wall of the duodenum into the head of the pancreas with involvement of a branch of the superior pancreaticoduodenal artery. The diagnosis of this lesion has become important, chiefly because the gastro-enterologists, with the aid of the flexible gastroscope, are attributing a high percentage of massive hemorrhages to gastritis or superficial gastric erosions. (Benedict,² in 1937, emphasized this point.) Since the posterior duodenal ulcer frequently bleeds without having shown any previous gastric symptoms (18 per cent of our 135 patients had a negative gastric history), one must, therefore, be sure to rule out a posterior duodenal ulcer before one attributes the cause of gastric hemorrhage to gastritis. More than one negative gastro-intestinal roentgenologic series should be obtained, the gastroscope is of no aid in making a diagnosis of posterior duodenal ulcer.

Patients who continue to bleed under medical management become the province of the surgeon. In these cases—the 10 per cent of massive hemorrhages which do not respond to medical care—operation during the acute stage may be a life-saving measure. The chief point of concern, naturally, is the selection of the patients who urgently require such operation.

In this respect blood transfusions may prove a helpful method of differentiation. Discussion still continues as to the advisability of transfusions during the acute hemorrhagic stage, but there seems to be no logical reason for delaying a transfusion, now that the “blood banks” and the general use of the citrate method have simplified the process. When the blood pressure has fallen to 80/60, the red cell count to 2,000,000 or less, and the hemoglobin to 35 per cent or thereabouts, it is obvious that the patient needs supportive measures. A transfusion is the best way of overcoming the shock and the reduced blood volume. In addition, the transfusion may be our lead as to whether to operate or to continue conservative measures.

If, after 500 cc of blood have been given, the red cell count, the hemoglobin, and the blood pressure remain low, one may assume that a large vessel has been eroded. If the procedure is repeated and there is still no improvement, it is fairly conclusive evidence that further delay may prove fatal. A continuous transfusion of 1,000 cc of citrated blood should then be started and the patient operated upon as soon as possible. Further delay at this time would probably result in a fatality.

The type of patient in whom transfusions are futile, and who requires operative intervention to avoid fatality, is illustrated in the following report

Case Report—A male, age 27, was admitted to the medical wards in March, 1937, for severe pain due to chronic duodenal ulcer. He had suffered from the ulcer for four years and had required hospitalization for three weeks in November, 1936. At the time of his readmission, his pain was severe and could not be controlled by a Sippy regimen. Two weeks of hospital treatment produced no improvement and the patient was, therefore, transferred to the surgical service.

While awaiting operation, he had a severe hemorrhage. Transfusion of 500 cc of blood by the citrate method was carried out immediately, and when, six hours later, his condition had not improved, a second transfusion was given. The following morning (10 hours after the second transfusion) his pulse was 130, blood pressure 65/55, red blood count 1,800,000, and hemoglobin 30 per cent. The patient was evidently in severe shock and had apparently lost ground during the 24 hours since the hemorrhage had begun—in spite of the two transfusions.

An immediate operation was advised, and 1,000 cc of blood were given in preparation. At operation a large posterior duodenal ulcer was found. The entire gastro-intestinal tract was filled with blood. A mass 20 cm in circumference, surrounded by marked edema and involving the head of the pancreas and the hepatic flexure of the colon, was encountered. A subtotal resection was performed. A perforated ulcer, 3 cm in diameter, was found on the posterior duodenal wall, and a bleeder was observed from one of the branches of the superior pancreaticoduodenal artery. The hepatic flexure was adherent to the mass and an area, 1x0.5 cm wide, had been eroded halfway through the wall of the intestine. Fortunately, the colon could be freed from the edematous pancreas, and the duodenal stump was closed with relative ease. The operation was completed by an anticolonic Polya anastomosis.

Immediately following the operation the patient was given 500 cc of blood. He had an uneventful convalescence and was discharged on the sixteenth postoperative day.

Comment—We feel that without surgery this patient would have died as a result of the hemorrhage, as active arterial bleeding was still evident at the time of operation. The two preoperative transfusions and their fruitlessness showed the necessity of immediate intervention and gave us the clue which saved the patient's life.

Operative Procedures—The type of operation to be performed depends on the location of the lesion. In the case of a gastric ulcer, simple excision may be sufficient. Unfortunately, however, most of these hemorrhages are due to ulcers of the mucosa on the posterior wall of the duodenum, and excision of a duodenal ulcer that involves the pancreas is seldom feasible.

We³ have also found that 15.5 per cent of our patients having had a subtotal gastrectomy for chronic duodenal ulcer had two ulcers, one anterior and one posterior. In such cases, the unfortunate mistake may be made of excising the anterior ulcer and leaving the posterior one, which is the real offender. We have encountered patients in whom this had occurred.

A gastrojejunostomy is of little aid in stopping or preventing the bleeding from a posterior ulcer. In a review of 106 cases of gastrojejunostomy, followed for seven years, we¹ found that 15, or 14 per cent, had been operated upon for massive hemorrhage, and that in 47 per cent of this group hemorrhage had recurred later. Of the 91 cases operated upon for pain without

hemorrhage, 165 per cent had massive hemorrhage following the gastrojejunostomy

The transduodenal operation with suturing or cauterization of the ulcer appears to be a rather unsurgical procedure, useful only in rare instances. We are dealing with a bleeder lying in a mass of inflammatory tissue and involving the head of the pancreas. Trying to suture and cauterize this area may be more dangerous than beneficial, for unless one single isolated vessel is encountered, the superior pancreaticoduodenal artery may be eroded by the cauterization.

Some surgeons feel that ligation of the gastroduodenal and the right gastro-epiploic artery may suffice to control the hemorrhage from an ulcer, but study of the blood supply to the first portion of the duodenum makes this seem a procedure of doubtful value. The supraduodenal artery, first described by Wilkie,⁵ in 1911, and confirmed by Reeves,⁴ in 1920, with its anterior and posterior branches, supplies the first one and one-half inches of the duodenum. It is essential to note the fact that this artery may arise from either the hepatic, the gastroduodenal, or the right or the left hepatic artery. This variable origin makes its localization difficult, if not impossible, in large ulcers with severe inflammatory reactions around the gastrohepatic and duodenohepatic omentum.

The most satisfactory method of attacking the bleeder appears to be by subtotal resection. In this one way, it is definitely possible to save a certain percentage of these otherwise doomed patients. The operation should be undertaken in all cases of massive hemorrhage where conservative measures are likely to fail. As indicated above, blood transfusions help to determine which these cases are. Lack of response to transfusion indicates the need for operative intervention.

COMMENT

Two blood transfusions of 500 cc each are given as a means of determining whether there is an arterial hemorrhage. If improvement does not occur, the patient should be operated upon in the stage of acute hemorrhage, while a continuous citrate transfusion is maintained. It is surprising how well the apparently hopeless case will withstand such a major surgical procedure as a subtotal resection.

REFERENCES

- ¹ Church, R. E., and Hinton, J. W. The Failure of Gastrojejunostomy in 106 Cases Followed for Seven Years. To be published.
- ² Benedict, E. B. *Tr. Am. Gastro-Enter. Assoc.*, 29-34, 1937.
- ³ Hinton, J. W., and Maier, R. L. Chronic Duodenal Ulcer. To be published.
- ⁴ Reeves, T. B. *Surg., Gynec. and Obstet.*, 30, 379-385, 1920.
- ⁵ Wilkie, D. F. D. *Surg., Gynec. and Obstet.*, 13, 399-406, 1911.

THE VALUE OF CECOSTOMY AS A COMPLEMENTARY AND DECOMPRESSIVE OPERATION*

FRED W RANKIN, M D

LEXINGTON, KY.

DECOMPRESSION of an obstructed colon by puncture or incision is one of the oldest operations in surgery. Littre, in 1710, first proposed colostomy for relief of obstruction due to malformation of the rectum. This bold suggestion, made about a century and a half before asepsis and anesthesia, lay fallow for 66 years until Pilloie, of Rouen, in 1886, performed a right inguinal cecostomy for relief of obstruction of the rectum due to a tumor.

In the development of surgery of the large bowel, the drainage operations have gone through successful evolutionary changes to the present-day type of colostomy and cecostomy, but the merits of the latter, both as a means of direct decompression and as a complement to extirpative surgical maneuvers aimed at malignant lesions of the lower gastro-intestinal tract, have received scant emphasis. One of the most important factors in the development of colonic surgery has been acceptance of the thesis that decompression either by surgical procedures or medical means is a highly important aid in returning a devitalized and desiccated patient, suffering from malignant disease, to a status approaching physiologic equilibrium.

When surgery is indicated, decompression may be easily accomplished in many cases by the employment of cecostomy. Moreover, this procedure is frequently desirable both as the first stage of a graded operation, and as a complement to an offensive for extirpation of cancer. The indications for cecostomy may be briefly summarized as follows:

- (1) A complementary measure following
 - (a) Obstructive resection,
 - (b) Resection and anastomosis of the intestine, end-to-end, or lateral,
 - (c) Exteriorization of a segment of the colon
- (2) Decompression for intestinal obstruction
 - (a) In acute obstruction secondary to cancer of the left colon or rectum,
 - (b) In subacute or chronic obstruction secondary to cancer of the colon or rectum unrelieved by medical measures
- (3) A planned first-stage of a graded operation

Complementary to Resection—Resection of the colon is usually accomplished by one of three types of operation, the choice depending upon the local conditions and the inclinations of the surgeon. They are (1) Resection and anastomosis, (2) obstructive resection, and (3) exteriorization. With the

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12,

first two types of resection, cecostomy may be employed routinely to advantage. Not infrequently exteriorization likewise is made safer and more simple by use of simultaneous collateral decompression. My own choice of operation for many years has been obstructive resection, and within the past five years the addition of complementary decompression has proved efficacious.

Obstructive resection was evolved because of dissatisfaction with some features of the exteriorization operation. In the main, these factors are: First, limitation of application, and second, transplantation of cancer cells into the cut surfaces of the abdominal wound (12 per cent of 183 cases reported in 1926). Obstructive resection utilizes the advantages of the exteriorization procedure, yet avoids this latter complication. Its usefulness was demonstrated in a series of 31 cases published in 1930. The criticism that it produced a complete intestinal obstruction for 48 to 60 hours, notwithstanding the fact that the obstruction was in the lower gastro-intestinal tract, was met by introducing routine complementary cecostomy. With this addition, it has become increasingly apparent that the convalescence is much more smooth, there is less distention, less elevation of temperature, and in general the post-operative course is benefited. The clamp may be allowed to remain on the ends of the bowel, at the point of resection, until it drops off, thus insuring against leakage and infection. The cecostomy tube is allowed to drain until the resection clamp drops off and then may either be pulled out or cut off and allowed to pass per rectum.

When resection and immediate anastomosis is accomplished, a primary consideration is relief of factors which influence wound healing unfavorably. Healing in a deliberate surgical wound of the colon is complicated by: First, infection, second, paucity of blood supply at the site of anastomosis, and third, tension on the suture line. The normal infection present in the bowel content is greatly reduced by preoperative preparation, but often not entirely relieved in the pericolic tissues where it migrates, due to increased permeability of the bowel wall, secondary to ulceration and obstruction.

The blood supply of the colon is consistent but scanty. The looping arcades which spread out fan-wise in the mesentery of the bowel are relatively constant in number as they ascend from the parent mesenteric vessels. Branches from these marginal vessels ascend as terminal arteries, tributaries which pass around the colon in a circular manner lying parallel to each other and perpendicular to the mesentery. This distribution leaves a small area on the antimesenteric border where the blood supply is feeblest and where distention from intraluminal pressure encroaches on the capillary bed to compromise the vascular tree and favor necrosis and rupture.

Primary wound healing, influenced enormously by the elimination of edema and infection through preoperative means and technical steps at resection, is further enhanced by elimination of the factor of distention. Surgical physiologists are unanimously agreed that during the first four to six days of wound healing, when the apposed surfaces are held together by mechanical means and buttressed by rapidly forming peritoneal exudate, cohesion is fragile and un-

certain During the next six to nine days fibroblast proliferation and organization increase the tensile strength of the anastomosis, but until the cicatrix is mature, union is vulnerable to increased intracolonic pressure Obviously distention of the colon which vitiates the blood supply or mechanically forces apart the cut wound margins facilitates leakage, and to prevent this, prophylactic decompression at time of resection is most useful This seems to be more easily accomplished by cecostomy than other means Appendicostomy is infinitely less useful because the appendix may be either absent from operation, atrophic, or retrocecal, and even when it is available, has a small lumen, inadequate for satisfactory drainage or irrigations

Table I illustrates the conditions for which complementary cecostomy was performed in my own practice during the past five years, together with the mortality, which in this series was 11.1 per cent

TABLE I
FORTY-TWO CASES OF COMPLEMENTARY CECOSTOMY

	No of Cases	No of Deaths
Obstructive resection	Cancer splenic flexure	1
	Cancer descending colon	2
	Cancer transverse colon	1
	Cancer sigmoid	30
	Diverticulitis	4
	<hr/>	
	38	
Exteriorization—Cancer colon	3	1
Presacral neurectomy—Megacolon	1	
	<hr/>	<hr/>
Totals	42	5

Decompression for Acute or Subacute Obstruction—Acute obstruction occurs in a high percentage of cases of cancer of the rectosigmoid and left colon and usually presents itself without premonitory symptoms All large clinics in urban centers are familiar with this type of acute intestinal obstruction and report its incidence in varying percentages Bugess,¹ of Manchester, reviewing a series of 485 cases of cancer of the colon, found 35.6 per cent of this group caused acute intestinal obstruction Meyer,² of Chicago, found that over a three-year period ending in 1937, 291 cases of cancer of the colon and rectosigmoid were admitted to the Cook County Hospital, and 75, or 25.7 per cent, were acutely obstructed upon admission

For relief of such obstruction, blind cecostomy, usually performed under local anesthesia through a split muscle incision in the right groin, is the procedure of choice In this connection, it may not be amiss to emphasize the advantages of performing a drainage operation without exploration of the abdomen There is little doubt that exploration and manipulation of acutely obstructed intestines multiply mortality rates Relief of the lethal obstruction may be followed during the convalescence by roentgenologic examinations to

CECOSTOMY

localize and identify the lesion, and surgical attack may be instituted at a later stage with a lower mortality

Cecostomy for immediate decompression is best performed by a different technic than when it is utilized as a complement to deliberate resection. For acute obstruction, it is desirable to bring the cecum or the ascending colon completely out of the abdominal cavity, thus by-passing the entire fecal cur-

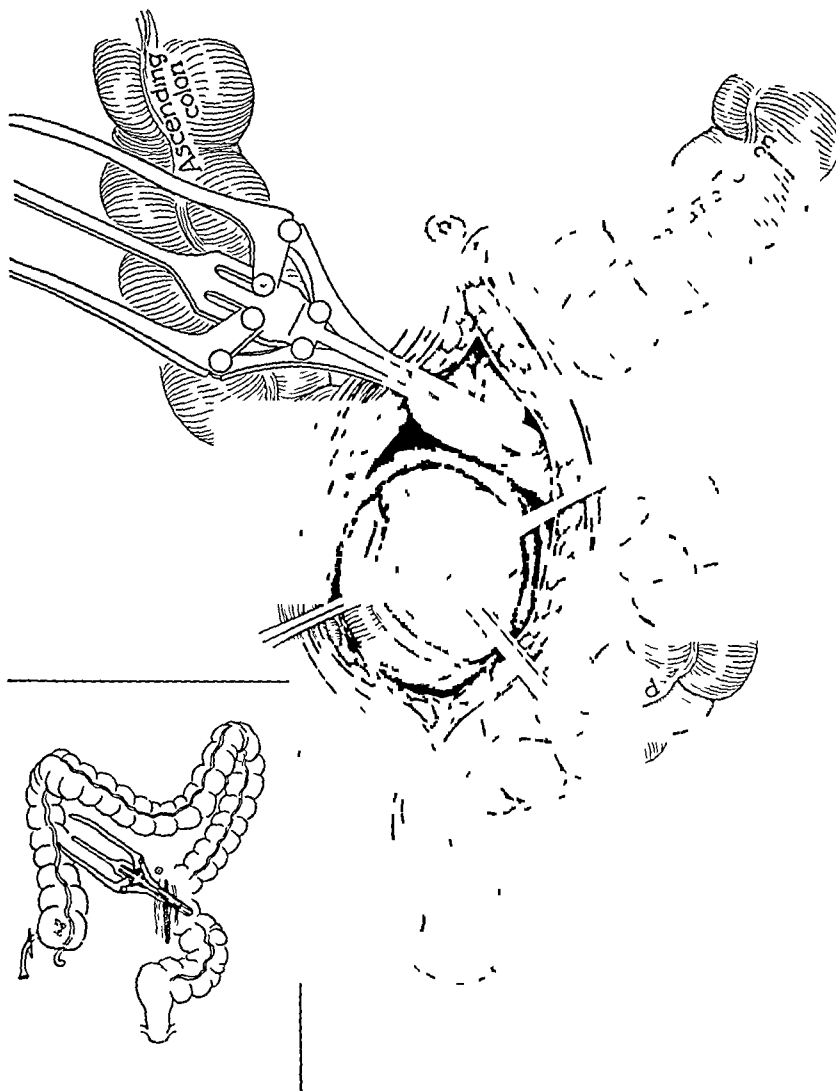


FIG 1—Shows an obstructive resection completed. The cecum is drawn out through the wound for the establishment of a complementary cecostomy. Purse string sutures are in place and the bowel is being punctured with the crutery. When the bowel is thoroughly decompressed there is no necessity for a rubber clamp. The inset shows the completed operation with the cecostomy tube drawn through a stab wound in the right groin.

rent. Subsequently, the opening is used to irrigate the bowel through and thus reduce the pericolic infection prior to resection. This procedure, simple as it seems and frequently is, when the cecum has a long mesentery and is not enormously distended, is actually, more often than not, a hazardous and difficult undertaking, and occasionally it becomes an impossible maneuver without partial decompression by puncture.

On opening the abdomen, in a case of acute obstruction of the colon, one

frequently finds a huge cecum, half filled with liquid feces and distended with gas to the point where its wall is as thin as tissue paper. Such an organ does not lend itself readily to manipulation without danger of rupture and peritoneal contamination. Efforts to suture this type of bowel to the peritoneum often result in decompression, for sooner or later the needle point will enter the bowel lumen and a whistle of gas announces the accident. It is better to seal

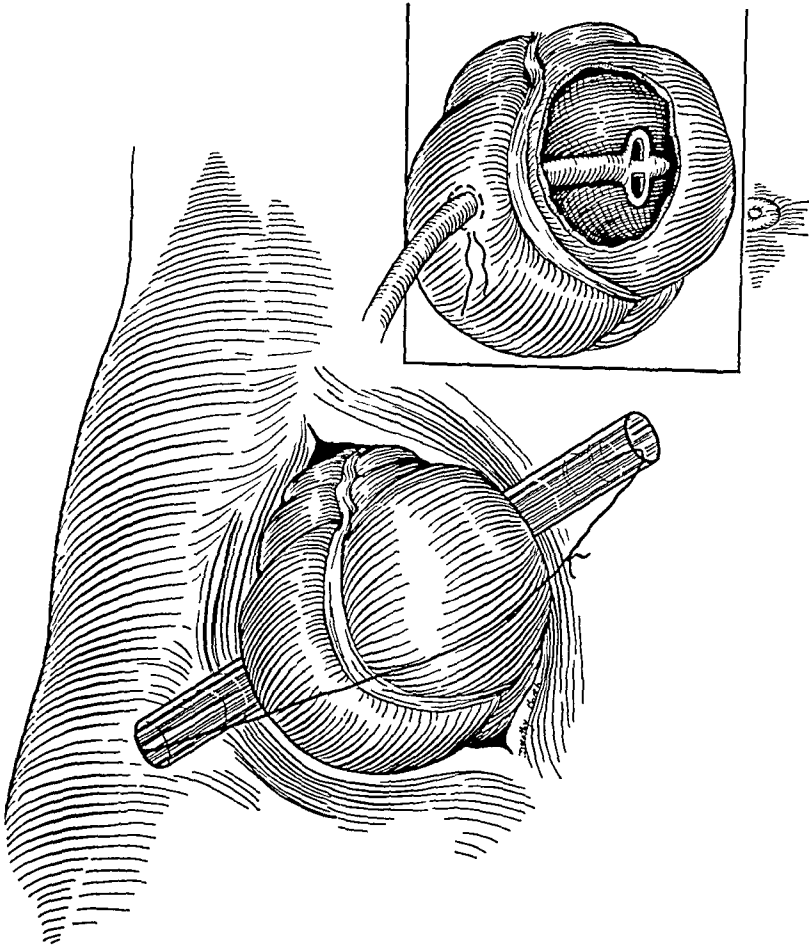


FIG 2—Shows the cecum completely exteriorized with a glass tube under it. This is desirable in acute intestinal obstruction, but if decompression is necessary before, the cecum may be drawn out and punctured with a needle. After the gas has been drawn off, a Pezzer catheter is inserted as shown in the inset. Complete by passing of the fecal current is thus established.

off the anterior bowel wall with packs as well as possible, and deliberately puncture the cecum with a small hypodermic needle, allowing the gas to escape. When the bowel has partially collapsed, the mucous membrane becomes flooded with blood, the entire bowel wall thickens and one may handle it then without fear of rupture. A choice may now be made between First, suturing a tube into the bowel, second, suturing the bowel to the peritoneum as Stone advises, or third, bringing the bowel out, closing the puncture wound and making a loop cecostomy.

Complete decompression of the colon under acute obstructive conditions is inadvisable and is occasionally followed by collapse just as in complete relief

of urinary obstruction. If it is impossible to perform a loop cecostomy for acute colonic obstruction and a tube is inserted into the bowel or the bowel is sutured to the peritoneum, a large tube should be used because irrigation with a small catheter is incompetent. There is small question that therapeutic rest, complete by-passing of the fecal current, and subsequent relief of the local and general effects of obstruction are best obtained by bringing out a loop of the right colon.

Recently in my service, cecostomy for the relief of acute intestinal obstruction has been performed 16 times. In eight of the cases, subsequent resection was impossible, and in the remaining eight, obstructive resection completed the procedure. The mortality in this group was high (18.7 per cent) because of the fact that half of the patients were so depleted when first seen that nothing more than decompression was possible.

TABLE II
SIXTEEN CASES OF CECOSTOMY FOR ACUTE INTESTINAL OBSTRUCTION

		No of Cases	No of Deaths
Followed by obstructive resection	Cancer transverse colon	3	
	Cancer sigmoid	3	
	Postoperative adhesions, large and small bowel	1	
	X-ray stricture descending colon	1	
		8	
Inoperable	Cancer sigmoid	2	1
	Cancer rectum	2	1
	Cancer rectosigmoid	1	
	Cancer left colon	1	
	Cause unknown	2	1
		8	3

Decompression of Obstruction Due to Rectal Cancer—The vast majority of rectosigmoidal cancers produce obstruction of some type. Preoperative medical management usually relieves this condition but occasionally at exploration one finds a thickened, hypertrophied bowel proximal to the growth, multiple telangiectases, engorged lymphatics, edema in the tissues of the mesentery, and other signs which definitely indicate a graded procedure. Under such circumstances, a cecostomy performed through a split muscle incision in the right groin makes an admirable first-stage of a graded maneuver. Whipple,⁴ in 1931, reported a number of cases carried out by this method, as a deliberate first-stage of graded operations for the graver risks. I have employed it in a number of instances where decompression had not been adequately accomplished prior to exploration and completed the operation at a subsequent stage by the perineo-abdominal radical maneuver. Under either condition, it may be used with satisfaction.

Disadvantages of Cecostomy—The main objection to the use of cecostomy is that an additional operative procedure is required for closure. Such an

operation may usually be carried out under local anesthesia and with slight discomfort to the patient or much additional loss of time in the hospital. Complementary cecostomy, if performed with technical accuracy, requires no secondary procedure. The tube is cut off and allowed to pass per rectum, or pulled out and the Witzelized cecum closes spontaneously and without prolonged drainage. It seems fair to affirm that the many advantages accruing from adequate drainage and irrigation outweigh whatever objections, economic or otherwise, may be offered.

CONCLUSIONS

(1) Cecostomy is a valuable adjunct to any type of resection of the colon. It prevents distention, moderates peristalsis, and promotes a smooth convalescence.

(2) Its usefulness as the first-stage of a graded operation for radical removal of rectal cancer has been demonstrated.

(3) Blind cecostomy for acute intestinal obstruction localized to the large bowel is a useful and often a life-saving operation.

(4) It is desirable to use different technics to perform cecostomy for its several indications. Complete by-passing of the fecal current by bringing out a loop of the cecum or right colon is superior as a means of decompression and irrigation prior to resection. For complementary cecostomy, however, where relief of distention by gas is the paramount factor, a wing-catheter introduced into the cecum by Witzel's technic is very satisfactory.

REFERENCES

- ¹ Burgess, A. H. Treatment of Obstruction of the Colon. *Brit Med Jour*, 2, 547-556 September, 1923.
- ² Meyer, K. A. Personal Communication.
- ³ Rankin, F. W. *Surgery of the Colon (Surgical Monographs)*. New York, D. Appleton & Co., 1926.
- ⁴ Whipple, Allen O. Advantages of Cecostomy Preliminary to Resections of Colon and Rectum. *J A M A*, 97, No. 26, 1962-1964, December, 1931.

DISCUSSION —DR HARVEY B. STONE (Baltimore). I think that Doctor Rankin has given a very comprehensive and fair statement of the views that most of us hold in regard to the value and utility of decompressive procedures and specifically of cecostomy. I think it is scarcely necessary in discussion to emphasize the points of agreement with the speaker, and I feel sure that most of us agree with him very largely in everything he has had to say.

There are two or three points in which it seems to me one might raise certain questions as to the universal application of what Doctor Rankin has had to say. In the first place, while everyone, I am sure, will agree as to the necessity of some decompressive procedure in cases admitted in the phase of acute, complete obstruction, I should like to call to your attention a difficulty that I once encountered in employing cecostomy. The case was a growth in the low descending colon. The patient recovered following cecostomy, which was of necessity performed without delivery of the cecum and was, therefore, not a completely by-pass cecostomy, because at the time of operation the cecum was in the condition, so graphically described by Doctor Rankin, in which any

attempt at complete delivery of the cecum would have resulted in disaster. It had to be a tangential cecostomy. Some 17 or 18 days later, an attack upon the primary growth revealed the fact that the colon between the cecostomy and the growth was full of feces, which rendered an attempt at radical removal of the tumor extremely difficult and almost impossible of decent handling.

The point that seems to me concerned in that particular case is that if the stoma had been placed closer to the point of obstruction—if, instead of a cecostomy, a transverse colostomy had been employed—the purposes in view would have been much more adequately obtained. That is, not only the primary purpose of decompression, but the secondary purpose of having a reasonably clean and empty bowel to deal with at the time of the definitive operation.

Another group of cases in which it seems to me simultaneous cecostomy, that is, cecostomy simultaneous with the resective procedure, may not necessarily be required, but in which the same purpose may be accomplished, are those cases of resection low in the sigmoid in which a tube may be passed up through the anus and rectum, through the anastomosis, and serve as a decompressive outlet, which, to my mind at least, seems quite as adequate as a cecostomy and has obvious advantages of its own.

Finally, it seems to me that in those cases to which Doctor Rankin has referred, which are neither completely obstructed on admission nor quite adequately relieved of their partial obstruction by preliminary preparation, I fully agree with him that in such cases a stage operation utilizing a cecostomy, or transverse colostomy, as I should prefer in that group of cases, is certainly a wise procedure.

DR ARTHUR W ALLEN (Boston) We have had such a satisfactory experience with cecostomy at the Massachusetts General Hospital that it seems worth while to mention it at this time. We are in complete accord with the principles set forth in Doctor Rankin's splendid presentation.

In the development of cecostomy in our hospital, Dr S J Mixter modified the Paul tube, a right angle glass tube with a flange which could be held within the bowel by a purse-string suture, and that method was used for a considerable length of time with a good deal of success. It had the disadvantage, however, that the tube would come out of its own accord in too short a time. Dr D F Jones then began to use a large rubber tube for this purpose. He frequently spoke of it as a tube as large as his finger or as large as his thumb, based on the experience of Doctor Gibson, of New York, who first advocated the rubber tube cecostomy for ulcerative colitis.

A modification of these two methods has been developed in our hospital, and I am going to show you a few lantern slides in a moment to demonstrate its application.

We have performed a total of 171 cecostomies for obstruction of some degree or preliminary to a second operation on the left bowel during the past 12 years. Some were performed at the time of left bowel resection, with suture as a complementary procedure. One hundred twenty of these have been performed by employing this modification of the Gibson technic, which will be described below, 21 by the Mixter tube alone, 21 by the Witzel technic, and nine by various other methods, such as exteriorization. There have been 19 deaths among these 171 patients. Eleven of these were due to carcinomatosis or perforation of the cancer prior to operation. Six deaths were undoubtedly due to errors in the technic of the procedure, and one to pulmonary embolus due to coronary occlusion. Of the 152 survivors only 12 needed closure of their cecostomies. That is one important feature of this method of

treatment There have been a certain number of postoperative herniae because this tube stays in place anywhere from two to three weeks through a McBurney incision

Operative Technic—The cecum is brought up, when possible, and delivered through the wound If it is markedly distended, as it so frequently is in obstruction, of course one cannot bring it out through the abdominal wall When it is distended, a suction trochar can be introduced and the cecum decompressed sufficiently to allow it to be grasped with Allis forceps, after which it may be delivered and a purse-string suture put in around the trochar opening

After the cecum has been collapsed somewhat, a rubber covered intestinal clamp can be placed on it below the opening, to prevent further soiling while the tube is inserted The large rubber tube which is fixed onto a right angle glass tube of approximately the same caliber—1 cm or more in diameter—is then inserted through the original purse-string and held in place by two additional purse-string sutures of No 0 chromic catgut, only the first one penetrates the rubber tube, to aid in the inversion of the cecal wall A tab of omentum, when available, is brought around the tube, and the cecum replaced within the abdomen

It is surprising how well one can clean out an obstructed colon by this method By the introduction of dilute magnesium sulphate into this tube after 48 hours, at various intervals, clamping the tube off for ten minutes or more until a peristaltic cramp takes place, one can fairly adequately clear out the proximal bowel Irrigations can frequently be carried out through the entire colon This method has been so adequate that proximal defunctioning procedures such as Devine has described, have very rarely been necessary in our clinic

The tube is brought out over above the iliac crest in a very comfortable fashion The rubber tube within the bowel will stay in place for two or three weeks with little or no leakage around it The rigid right angle glass tube in the abdominal wall prevents the kinking of a rubber tube alone Infection in the abdominal wound invariably takes place but has produced no serious or insurmountable sequelae

RETROPERITONEAL CHYLE CYSTS^{*}

WITH ESPECIAL REFERENCE TO THE LYMPHANGIOMATA

JOHN C A GERSTER, M D

NEW YORK, N Y

THE majority of retroperitoneal chyle cysts are rare forms of cystic lymphangiomata. Before directly considering the cysts themselves, a brief consideration of benign lymph vessel tumors may be of interest.

According to Most³⁸ and many others, a lymphangioma is a tumor arising from new growth of lymph vessels, as well as a widening of lymph vessels normally present. It is chiefly characterized by growth of the smaller, and even of the capillary lymph vessels. Besides, a true lymphangioma may arise from lymph nodes through new growth arising in intraglandular sinuses and adjacent lymph vessels. Certain lymphangiomata are obviously of congenital origin. Others make their first appearance in adult life. Stasis alone does not, in itself, constitute an adequate causative factor—the plentiful collaterals easily furnish a by-pass.

According to Ribbert,⁴⁴ a lymphangioma is a new growth of lymph vessel walls and their adjacent connective tissue. The neighboring normal lymphatics have few or no connections with the lymphatic new growth. The surrounding connective tissue is just as active in its growth, if, indeed, not more so, than the lymph vessels themselves.

The sites of predilection are the skin and subcutaneous tissues, especially around the face, the neck, the inguinal region (including spermatic cord and ligamentum rotundum), the retroperitoneal region, the mesentery, and even the intestine itself.

The three types mentioned below (Wegner⁶⁵) do not always appear clear-cut—transition forms are noted.

(1) Lymphangioma Simplex, according to Most, is a transition form between lymphangiectasis and a true lymphatic tissue tumor. It is a circumscribed swelling with an ill-defined margin, composed of dilated lymph vessels, with an actively growing, richly cellular, connective tissue stroma. It is usually seen in infants and children, involving the skin and subcutaneous tissue of face or neck. It is compressible.

(2) Lymphangioma Caveinosum (a sharp line between lymphangioma simplex, and lymphangioma caveinosum cannot always be drawn) is a spongy tumor, composed of dilated lymphatic vessels, with a lymphoid stroma in an actively growing condition. Clinical examples are macromelia (lymphangioma of the cheek), macrocheilia (lymphangioma of the lip), macroglossia (lymphangioma of the tongue). Other regions of involvement may be the eyelids, neck, gums, pharynx, inguinal regions, the mesentery of the intestine,

^{*} Read before the New York Surgical Society, November 9, 1938. Submitted for publication October 26, 1938.

and the retroperitoneal regions. The overlying skin or mucous membrane is not usually involved. The tumors are more obvious than lymphangioma simplex. They are spongy and compressible.

(3) *Lymphangioma Cysticum*. While the two forms noted above may have some connections with the adjacent normal lymph vessels, the cystic form has practically none in the majority of cases. The walls are composed of connective tissue with numerous endothelial-lined lymph spaces, which in some areas show cavernous development. Besides connective tissue, smooth muscle fibers are present, and more or less lymphoid infiltration. The cyst may have an endothelial lining, however, it may be partly or completely absent (see below). The contents may be a serous or a chylous fluid. There may be blood, consequent upon trauma. Cystic lymphangiomata are not compressible, are more or less encapsulated and, as just said, may have almost no connection with near-by lymphatics.

Sites. In the neck they may be superficial or deep, they also occur in the supra- or infraclavicular regions, the axillae, the inguinal regions, and the mesentery, and retroperitoneal regions, where they often contain chyle.

Lymph cysts and chyle cysts of the abdomen arise from lymphatics of the retroperitoneal region, or from the chyle-bearing lymphatics of the intestine. They may start retroperitoneally, and push forward between the leaves of the mesentery, or vice versa. The mesenteric forms are by far the more frequent. The retroperitoneal forms are much rarer. Typical intra-abdominal and retroperitoneal cavernous lymphangiomata have been observed. Consequently, lymph and chyle cysts may arise from these. Transition forms occur.

A history of trauma has been noted in a number of cases. However, considering the frequency of trauma and the great rarity of cysts, trauma as a cause seems unlikely although trauma to a hitherto "silent" cyst may be a factor in inaugurating renewed growth. The so-called blood cysts of older authors have proven to be either preformed cysts (lymphatic, dermoid, enterocystomata, etc.) filled with blood, or encapsulated hematomata.

A cystic lymphangioma may have a cavernous angioma at some point in its periphery. Pathologists (beginning with Wegner) have held that the cystic form developed from the cavernous, that in examining a cystic tumor to obtain reliable evidence of its origin often this is difficult or even impossible, that presence of the cavernous areas in the cyst wall itself or near by in adjacent tissues, points either to association of the two forms or to the cystic, originating from and overgrowing, and so partly obliterating, the cavernous portion. Lastly (as said before), dilated lymphatic vessels leading to, or away from, a cystic lymphangioma may be either part of (extensions of) the benign new growth or lymphangiectatic dilatations of pre-existing (normal) lymph vessels due to pressure from the cyst. Even under the microscope this may be hard to determine.

In thicker-walled cysts three distinct layers have been described by various authors. An endothelial lining may be present as a single layer of cells, or it

may be partly absent or may be entirely lost. The absence of endothelial lining has been so frequently observed that certain authors considered this a characteristic feature. This absence has been ascribed, with reason, to the ease with which a single layer of cells might be rubbed off in the course of operative removal or in handling of the fresh specimen. On the other hand, its absence has been noted in unopened cysts removed in toto and hardened as such, before cutting for microscopic examination, the endothelial and inner layers of the cyst wall had undergone fatty and hyaline degeneration. In thinner-walled (younger?) cysts from the same specimen the endothelial lining was present intact (Godel¹⁸).

Chylous Contents—Chyle cysts refill slowly after aspiration. Chyle cysts, marsupialized, do not drain chyle—they usually heal in a few weeks with moderate discharge of serous exudate. Excision of chyle cysts is not followed by escape of chyle from cyst bed. All this seems good clinical proof that chylous lymphangiomata have little or no connection with adjacent normal chyle-bearing lymphatics.

Whence the chylous fluid? Either it comes from a very slight connection with normal chyle-bearing lymphatics or from chyle-like accumulation (transudation) from the cyst wall itself with its rich blood and lymphatic supply, in combination with a fatty and hyaline degeneration of the inner coats (Henschen²³).

As a matter of interest, "chyle-containing" cystic lymphangiomata have been observed in the neck (Volkmann⁶³), in the groin, and in the extremities (Henschen and others)—sites distant from normal chyle-bearing lymphatics.

Studies of fat content in the lymph collected from lymph fistulae of the lower extremities have shown variations almost identical with those observed in chyle itself: from 0.6 to 2 per cent during hunger periods to as high as 47 per cent after a fatty meal (Henschen).

Symptoms—There may be none. The first lymph and chyle cysts to be reported were chance finds at autopsy. If symptoms are present, a gradual onset is the rule. There are loss of weight, vague digestive disturbances, increasing constipation in some cases, an increase in the size of the abdomen, and a feeling of tension. The tumor which is present is not movable (retroperitoneal). Usually it lies above the umbilicus, to the right or left of the midline. A consideration of age and sex (four times as frequent in females as in males) has little significance. Statistics are of little aid when considering an individual case.

Diagnosis—In very small tumors no diagnosis is possible. In very large tumors, especially those almost filling the entire abdomen, these lymph and chyle cysts have been mistaken for ovarian cysts. This was particularly so in the early cases (in the 1880's). When aspiration through the intact abdominal wall revealed their contents as chyle, in some instances as much as 3,000 or 4,000 cc at a time was repeatedly drawn off. The medium-sized *mesenteric* cysts, the size of a child's head, or perhaps larger, have to be differentiated from other forms of intra-abdominal cysts.

With the *retroperitoneal* cysts, an exact diagnosis is impossible, but by modern roentgenographic visualizing methods, the various adjacent viscera may be demonstrated as normal, and their anatomic relationship to the intra-peritoneal or retroperitoneal tumor may be determined. Even after celiotomy and either removal or marsupialization, the exact diagnosis must wait upon the microscopic character of the cyst wall *

Prognosis depends on the patient's general condition at the time of operation, and the mechanical ease or difficulty of removal or marsupialization.

Treatment—Excision is the method of choice, if mechanically feasible. At celiotomy, a preliminary aspiration of part or all of the contents often has facilitated subsequent removal of the cyst wall. No leak of chyle following excision is to be expected, although when in doubt, drainage with a soft rubber dam to the cyst's bed may be considered safer.

Marsupialization is indicated where excision entails too great a risk. Marsupialization has been performed both transperitoneally and through lumbar incisions, depending on the accessibility of the particular cyst. Marsupialization has not been followed by excessive chylous drainage in the majority of cases. Healing usually has occurred within two to four weeks. Exceptionally, excision of cyst wall, secondary to marsupialization, has been necessary because of a persistent sinus.

The following case of a retroperitoneal chyle cyst is of interest because the cyst was actually visible roentgenologically.

Case Report—A C, female, age 34, single. Six years ago, she had had an appendectomy performed by the writer for acute suppurative appendicitis, an uneventful convalescence followed. On February 14, 1938, the patient, referred by Dr M C L McGuinness, was admitted to the Lenox Hill Hospital, New York, with the following history.

She had been well since her appendectomy until July, 1937, eight months before, when she "awoke one night with a feeling of chilliness, as if a wind had blown on her neck." A few days later began to have a band-like pain in the small of the back at the waistline. This had no reference to eating, standing or walking. The pain lasted ten days, then disappeared. Two weeks ago the same pain, starting in the back and right lumbar region and radiating forward with band-like sensation, reappeared. The pain increased in area and then moved forward toward the anterior abdomen, also extended somewhat to the left. During the past month there had been increased difficulty in function of the large bowel, there was constipation and even flatus could not be expelled, enemata were constantly required to effect a movement. There was no loss in weight. Appetite always good.

Traumatic History—A fall on the coccyx, at age 14, was followed by some pain and discomfort for a while. One and one-half years ago, she fell, striking the left

* As said at the beginning of this article, most retroperitoneal cysts are cystic lymphangiomas, less frequently they prove to be dermoids, hydronephroses (Koblanck and Pforte³³), cold abscesses, etc. A consideration of all these other forms of retroperitoneal cysts is too extensive a subject to be included within the scope of this article. Handfield-Jones²⁹ classification of retroperitoneal cysts is given in the appended bibliography. Various classifications and theories of pathogenesis are to be found in nearly all of the other articles listed.



FIG 1—Plain roentgenogram showing a shadow of the tumor to the right of the first, second, and part of the 3rd lumbar vertebrae



FIG 2—Roentgenogram showing the transverse colon lying below the tumor while another exposure (Fig 3) shows it lying above the tumor



FIG 3—Roentgenogram showing the transverse colon lying above the tumor, while another exposure (Fig 2) shows it below the tumor



FIG 4—Roentgenogram showing lateral compression of an apparently normal, dye-filled gallbladder

epigastrium, left breast and axilla. Pain in this region lasted for several months, then disappeared.

Physical Examination was negative except for a smooth nonmovable mass in right hypochondrium which gave impression of a tense, distended gallbladder. It was sufficiently prominent to push the overlying abdominal wall slightly forward, as seen by reflected light in comparison with opposite (left) hypochondrium. Upon pressure on this tumor, the pain in the back at this level was increased. The mass did not move with respiration, and was not, in itself, tender.

White blood count was normal, except for 6 per cent eosinophils on first count, 1 per cent eosinophils later, otherwise entirely negative. Red blood count was normal. Blood chemistry, normal. Blood pressure was within normal limits. Urinalysis was normal.

Roentgenologic Examination of chest was normal. A plain roentgenogram of the abdomen (Fig 1) showed the shadow of a soft tissue mass, approximately 10 cm

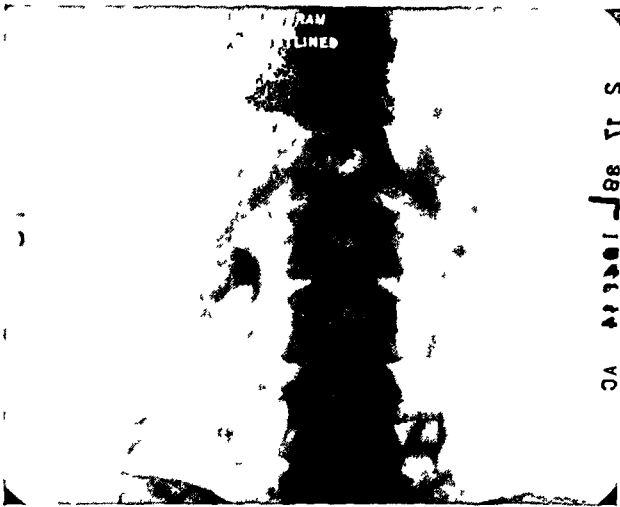


FIG 5—Roentgenogram following intravenous urography showing normal bilateral excretion and good visualization of the calices, pelves and upper ureters on both sides. The mass is to be seen overlying the right kidney pelvis.

in diameter, lying to the right of the spinal column opposite bodies of the first, second, and upper part of the third lumbar vertebrae. The bony spine was normal. The kidney shadows were normal in size, shape and position, and were well visualized.

Barium enema showed normal colonic outline. In some views the transverse colon was below the mass (Fig 2), in others above it (Fig 3).

The dye-filled gallbladder, at the fortieth hour, was visualized, and appeared indented and displaced to the right by the soft tissue mass (Fig 4). The concentration and emptying of

the gallbladder were demonstrated to have been normal as seen roentgenologically.

Intravenous urography showed normal excretion of dye from both kidneys with good visualization of calices, pelves, and upper ureters on both sides. The right kidney pelvis of normal outline lies directly behind the tumor mass (Fig 5).

A gastro-intestinal series showed the stomach to be J-shaped and displaced somewhat to the left. The stomach and first portion of duodenum were normal in outline. The second portion of the duodenum, both under fluoroscopy and in the films, showed evidence of marked compression by the mass. The duodenum was displaced anteriorly and to the left (Fig 6). This did not cause actual obstruction—the stomach was empty at three hours. Oblique views showed the descending portion of the duodenum pushed forward by tumor (Fig 7).

Roentgenologic Inferences—The findings indicated a retroperitoneal mass in the right upper quadrant lying alongside and partly overlying the first, second, and part of the third lumbar vertebrae. "It (the mass) does not have the characteristic appearance of an expanding lesion in the head of the pancreas, which generally displaces the descending portion of duodenum to the right."

Among other preoperative diagnoses the following were considered: Neurogenic sarcoma, tumor of right adrenal, and retroperitoneal dermoid. Normal bony spine outlines seemed to exclude a cold abscess of spinal origin.

Operation—February 23, 1938. The abdomen was opened through a five-inch, longi-

tudinal, right paramedian, epigastric incision To obtain more room, a transverse incision three and one-half inches long was added, beginning at the lower end of the longitudinal incision, and going to the right (Fig 8 A)

Operative Pathology—The tumor was immediately apparent, lying behind the hepatic flexure of the colon at the beginning of the transverse colon On displacing the colon downward, the flattened-out second portion of the duodenum was seen lying over the tumor (Fig 8 B) Both it and the posterior parietal peritoneum were freely movable upon the underlying tumor This peritoneum was divided longitudinally along the outer side of colon and duodenum (Fig 8 B), which were then retracted mesially The tumor was the size of an adult fist, and was now free except for its posterior attachment It was attached to the anterior aspects of the bodies of first and second lumbar vertebrae between the aorta and the inferior vena cava The aorta was entirely free, but the inferior vena cava was intimately adherent to the right side of the tumor

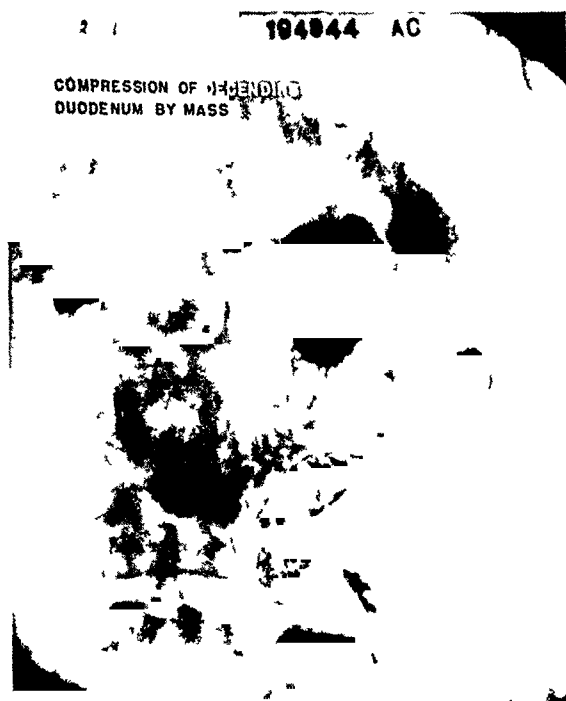


FIG 6—Roentgenogram showing compression of the descending duodenum by the tumor



FIG 7—Roentgenogram, taken obliquely showing pressure posteriorly upon the duodenum by the tumor

for a distance of three inches (Fig 8 C and D) The tumor was dark reddish-blue in color and seemed solid Attempted dissection of tumor from vena cava proved impractical and too hazardous Upon aspiration, using a large caliber needle, a thick milky fluid was immediately obtained After removal of about 20 or 30 cc, the needle became clogged

The tumor was incised longitudinally As the outer wall was being divided, an inner layer began to protrude A plane of cleavage was readily found The cyst was now more widely opened, its remaining fluid contents removed with an aspirator, and a few white clots were sponged out The inner lining was completely enucleated, exposing the tendinous origins of psoas attachments to first and second lumbar vertebrae The redundant outer cyst wall was then trimmed away except that portion attached to the inferior vena cava Two soft-rubber Penrose drains were inserted in the bed of the cyst and brought out through a stab wound lateral to the right rectus margin Duodenum and colon were replaced in their normal positions Closure of entire wound in layers Dry dressing

Postoperative Course—Uneventful convalescence No drainage of chyle came from the wound at any time Drainage tubing gradually shortened Primary union Dis-

charged March 28, 1938, 33 days after operation Postoperative roentgenologic examination of duodenum showed a normal outline (Fig 9)

Subsequent Course—During the next four months she was subject to attacks of upper abdominal pain, having no relation to meals At times there would be a premonitory feeling one-half hour before the actual attack At other times there would be a sudden severe pain in the upper abdomen lasting for two or three minutes, of such severity that physical movement was impossible Atropine sulphate gr 1/150 was given

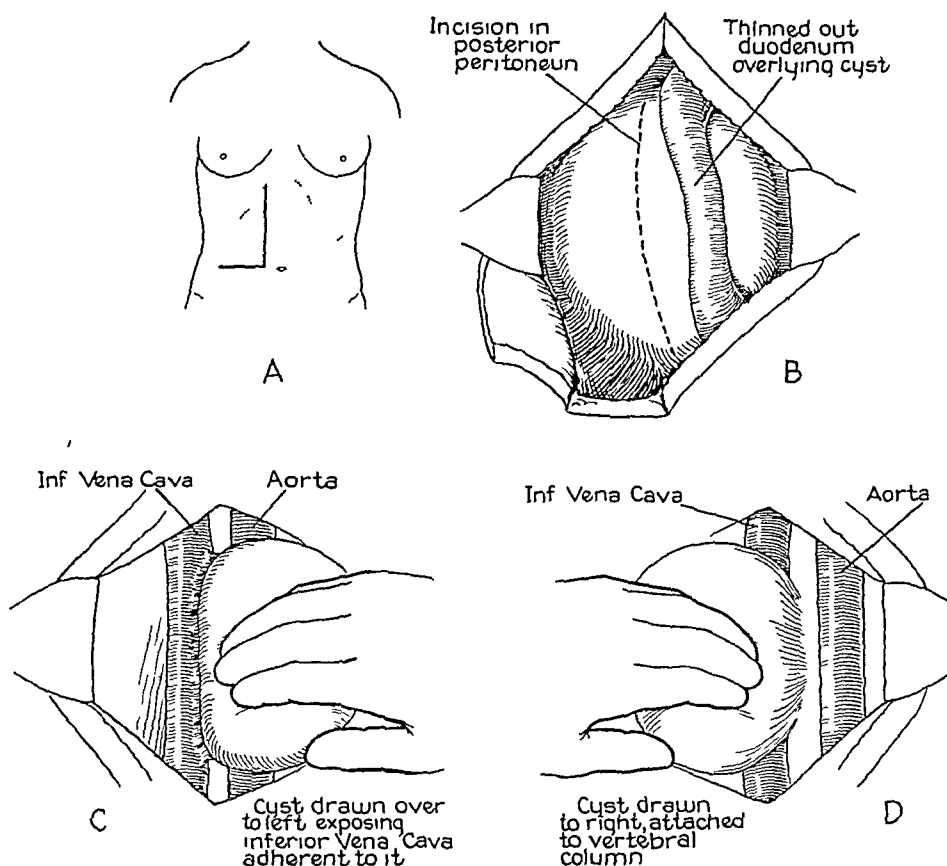


FIG 8—(A) Abdominal wall incision (B) Tumor presenting in wound with flattened descending duodenum overlying it The dotted line indicates incision postparietal peritoneum (C) Cyst drawn to the left, showing its dense adhesion to inferior vena cava (D) Cyst drawn to the right showing attachment to anterior vertebral column Aorta lies to the left, not adherent

by mouth and the dose had to be repeated 20 minutes later The pain would gradually subside in about two hours, but the abdomen would be sore and sensitive to touch for the next 24 hours According to the patient, "It would usually take five to seven days for the intestines to become normal again"

At first the attacks came every week or ten days but gradually the intervals between lengthened The last attack was at the end of July, 1938 There have been none since then—three months During the four months just described, there was constant belching, but none since Appetite has always been good

Examination of the fluid aspirated from the cyst showed by direct smear no organisms, no pus cells "Amorphous material with many fat-like globules giving partial fat reaction, with Sudan 3—a milky fluid" Culture sterile *Chemical Examination* Calcium content of the fluid showed 34 mg per 100 Gm (The calcium content of human milk averages 33 mg per 100 Gm) This calcium content possibly accounted for visibility of cyst roentgenologically

Pathologic Examination—Dr Rudolf M. Paltauf *Gross* "The specimen received consists of a roughened, pink, ovoid sac which has been cut into and contains cheesy, friable, necrotic white material. It is 7.5 cm with a wall 1 mm thick. The external coat is dull, roughened and pink, while the internal coat is dull, roughened and white and covered with necrotic, cheesy, friable material.

"*Microscopic Examination* (H and E stain) reveals the cyst wall, although greatly distorted, to consist of three more or less distinctly different layers. The inner surface is partly covered with pale, bluish-pink staining, slightly granular, amorphous material which also fills the cavity and contains scattered erythrocytes and large round cells with a foamy cytoplasm and small round, centrally situated nuclei, occasional cholesterol crystals are also present. The lining consists of flattened endothelial cells which are often missing. The inner layer is formed by hyalinized material which is fibrillar in character and shows fibroblasts and scattered round cells. In the middle layer, which is composed of more cellular and less degenerated connective tissue, there are many smooth muscle bundles which occasionally form quite a thick layer, covering this toward the outside is a third layer of connective tissue which is rather loose and infiltrated with fat and contains many blood vessels, infiltrated with small lymphocytes and plasma cells. In one section, it contains a well circumscribed area of lymphoid tissue which is represented by many definite lymph follicles. It shows slight interstitial fibrosis and hyperplasia of the reticulo-endothelial cells. The sinusoids are wide and filled with large endothelial cells, erythrocytes and a few lymphocytes. These three distinct layers are not everywhere recognizable, as they are frequently obscured by irregular areas of fibroblastic proliferation, round cell infiltration, fresh and old hemorrhages, evidenced by large extravasations of blood, and areas containing numerous large phagocytic cells loaded with hemosiderin pigment. Some of these hemorrhagic areas are quite extensive and undergoing organization.

"*Pathologic Diagnosis*—The cyst represents a chyle cyst which was the site of apparently repeated traumatic hemorrhages. The origin of the cyst may be either congenital or on a benign neoplastic basis."

SUMMARY—A female, age 34, suffering from pain in small of back and constipation of one month's standing, presented a tumor suggesting a distended gallbladder. The tumor gave a visible shadow roentgenologically. By appropriate visualizing methods, it was shown to be retroperitoneal, in front of the right kidney, behind the duodenum, to the left of the gallbladder (indenting it) and not attached to the hepatic flexure or the transverse colon.

At operation, it was found to be a thick-walled cyst containing creamy white fluid, with a capsule densely adherent to the inferior vena cava and (to the left) less intimately to anterior aspects of the first and second lumbar vertebrae. **Excision Recovery**



Fig 9—Postoperative roentgenogram showing a normal outline of the duodenum

Pathologic examination of the contents of the cyst revealed chyle-like fluid of the same calcium content as human milk, which probably accounted for visibility of cyst roentgenologically Culture sterile

Microscopic examination of cyst wall showed connective tissue, smooth muscle, lymph spaces lined with endothelium, lymph follicles, a partly missing endothelial lining, *etc*, typical of cystic lymphangiomata (chylangiomata)

The origin of the cyst may be either congenital or on a benign neoplastic basis

CONCLUSIONS

- (1) Intra-abdominal chyle cysts are surgical rarities
- (2) Retroperitoneal chyle cysts are much more rare than the mesenteric variety
- (3) The site, size and relation of sizable cysts to adjacent viscera may be demonstrated by modern roentgenographic methods
- (4) The exact diagnosis is determined by the microscopic character of the cyst wall (lymphangioma, dermoid, hydronephrosis, *etc*) Analysis of the fluid contents is of secondary interest
- (5) Excision is the method of choice, but if likely to be attended by too great risk of injury to vital structures (blood vessels, intestines, *etc*), marsupialization is indicated and has given good results

FOREWORD TO BIBLIOGRAPHY

To gain a proper idea of chyle cysts has entailed an extensive review of the literature dealing with both the mesenteric and the much rarer retroperitoneal forms Chyle cysts are rare—many surgeons of wide experience have never encountered one—yet there are approximately 500 reports in the literature Probably because of their rarity, nearly all cases have been reported

Titles at times have proven inaccurate, cysts reported as mesenteric might with equal reason have been classified as retroperitoneal Reports have been incomplete, specimens of the cyst wall were not taken or, if taken, were lost or, even if examined, the gross and microscopic descriptions were not given in detail The same applies to information about the contents of the cysts

Regarding information about the exact size of cysts, in some cases, it must be admitted, this was impossible, especially in huge irreducible cysts, particularly if found in obese subjects

The author has made no attempt to furnish a complete bibliography Articles of particular interest from one point or another (historic, pathologic, clinical) have been given—in many cases, brief abstracts or excerpts have been included for the reader's convenience To those interested in following the subject further, especially regarding the theories of pathogenesis, classification and detailed microscopic examination, the articles by Braquehay⁴ (1892), Dowd¹⁰ (1900), Smolei⁵³ (1901), Sick⁵⁰ (1902), Klemm³² (1905),

Speckert⁷⁴ (1905), Henschen²³ (1905), v Hippel³⁰ (1909), Prutz and Monnier⁴² (1913), Hadley¹⁹ (1916), Most³⁸ (1917), Godel¹⁸ (1921), Handfield-Jones²⁰ (1924), Swaitley⁵⁷ (1927), and Ebhardt¹¹ (1932) will be found of especial interest

Aside from periodicals on general surgery, here and there in the publications devoted to pathology (Vichows Archivs, for example), embryology, urology, pediatrics, and gynecology, articles occur bearing upon the subject of this paper

BIBLIOGRAPHY

¹ Bauer Uber Mesenteriale und retroperitoneale Cysten Beitr Z klin Chir, 70, 829, 1910

² Benedict, A L Bibliography of Chylous Cyst of the Mesentery Surg, Gynec, and Obstet, 16, 606, June, 1913

³ Bramann, P Uber chyluscysten des mesenteriums Arch f klin Chir, 35, 201, 1887
Male, 63, operated on by von Bergmann (April, 1886) Cyst occupied mesentery of almost entire small intestine, 800 cc creamy fluid aspirated, marsupialized (just managing to avoid intestinal walls), palpating finger reached to spine—interior of cyst smooth Recovery Microscopically, connective tissue, blood vessels, no endothelial or epithelial lining Author notes (1) Intestine and its lymphatics were entirely normal, (2) aspirated cysts refill, (3) drained (marsupialized) cysts heal

⁴ Braquehaye, Jules Des Kystes du Mesentere Arch Gen de Med, 2, 291 and 572, 1892

A carefully written, comprehensive monograph covering historic, statistical, pathologic and clinical aspects to date Braquehaye's statement—that Benevieni, the Florentine anatomist, was the first to observe a mesenteric cyst, in 1507—has been quoted ever since Fine bibliography, but misses a number of important early German references

⁵ Broca, A et Daniel, C Les kystes du mesentere dans l'enfance Rev de Gyn et de Chir abdominale, 9, 447, 1905

⁶ Carson, N B Chylous Cyst of Mesentery J A M A, 14, 674, 1890
Male, 39 Tumor size of a fetal head, between umbilicus and pelvis, diagnostic aspiration, chyle obtained Then three years elapsed Operation, five pints of chyle evacuated, marsupialization Recovery No description of operative findings, location of cyst, etc First American report of chyle cyst of mesentery

⁷ Collins, A N, and Berdez, G L Chyle Cysts of Mesentery Arch Surg, 28, 335, 1934

⁸ Crane, W Lymphangioma of Mesentery Am Jour Surg, 9, 441, 1930

⁹ Carter, R M Cysts of Mesentery Surg, Gynec, and Obstet, 33, 544, 1921

¹⁰ Dowd, Charles N Mesenteric Cysts ANNALS OF SURGERY, 32, 515, 1900

A comprehensive review to date Dowd (p 531) says " Chylous cysts are really preformed cysts situated in such close relation to the lacteals that chyle has been effused into them and that they are really embryonic in origin, in structure similar to ovarian and parovarian cysts "

This paper attracted wide attention, and with reason It was the first authoritative contribution on the subject in this country

¹¹ Ebhardt, K Beitrag zur Frage der Chyluszysten Bruns Beitr z klin Chir, 156, 103, 1932

The most recent comprehensive monograph, it differs little, if any, with that of Henschen, in 1905 Both cover the subject thoroughly

Male, 3½ Entire abdomen filled by tumor Contrast roentgen ray studies of colon and kidneys proved them normal Cyst freed from great omentum and gas-

Pathologic examination of the contents of the cyst revealed chyle-like fluid of the same calcium content as human milk, which probably accounted for visibility of cyst roentgenologically. Culture sterile.

Microscopic examination of cyst wall showed connective tissue, smooth muscle, lymph spaces lined with endothelium, lymph follicles, a partly missing endothelial lining, *etc*, typical of cystic lymphangiomas (chylangiomas).

The origin of the cyst may be either congenital or on a benign neoplastic basis.

CONCLUSIONS

- (1) Intra-abdominal chyle cysts are surgical rarities.
- (2) Retroperitoneal chyle cysts are much more rare than the mesenteric variety.
- (3) The site, size and relation of sizable cysts to adjacent viscera may be demonstrated by modern roentgenographic methods.
- (4) The exact diagnosis is determined by the microscopic character of the cyst wall (lymphangioma, dermoid, hydronephrosis, *etc*). Analysis of the fluid contents is of secondary interest.
- (5) Excision is the method of choice, but if likely to be attended by too great risk of injury to vital structures (blood vessels, intestines, *etc*), marsupialization is indicated and has given good results.

FOREWORD TO BIBLIOGRAPHY

To gain a proper idea of chyle cysts has entailed an extensive review of the literature dealing with both the mesenteric and the much rarer retroperitoneal forms. Chyle cysts are rare—many surgeons of wide experience have never encountered one—yet there are approximately 500 reports in the literature. Probably because of their rarity, nearly all cases have been reported.

Titles at times have proven inaccurate, cysts reported as mesenteric might with equal reason have been classified as retroperitoneal. Reports have been incomplete, specimens of the cyst wall were not taken or, if taken, were lost or, even if examined, the gross and microscopic descriptions were not given in detail. The same applies to information about the contents of the cysts.

Regarding information about the exact size of cysts, in some cases, it must be admitted, this was impossible, especially in huge irremovable cysts, particularly if found in obese subjects.

The author has made no attempt to furnish a complete bibliography. Articles of particular interest from one point or another (historic, pathologic, clinical) have been given—in many cases, brief abstracts or excerpts have been included for the reader's convenience. To those interested in following the subject further, especially regarding the theories of pathogenesis, classification and detailed microscopic examination, the articles by Braquehay⁴ (1892), Dowd¹⁰ (1900), Smolei⁵³ (1901), Sick⁵⁰ (1902), Klemm³² (1905),

Speckert⁵⁴ (1905), Henschen²³ (1905), v Hippel³⁰ (1909), Prutz and Monnier⁴² (1913), Hadley¹⁹ (1916), Most³⁸ (1917), Godel¹⁸ (1921), Handfield-Jones²⁰ (1924), Swaitley⁵⁷ (1927), and Ebhardt¹¹ (1932) will be found of especial interest

Aside from periodicals on general surgery, here and there in the publications devoted to pathology (Virchows Archivs, for example), embryology, urology, pediatrics, and gynecology, articles occur bearing upon the subject of this paper

BIBLIOGRAPHY

¹ Bauer Uber Mesenteriale und retroperitoneale Cysten Beitr Z klin Chir, 70, 829, 1910

² Benedict, A L Bibliography of Chylous Cyst of the Mesentery Surg, Gynec, and Obstet, 16, 606, June, 1913

³ Bramann, P Uber chyluscysten des mesenteriums Arch f klin Chir, 35, 201, 1887
Male, 63, operated on by von Bergmann (April, 1886) Cyst occupied mesentery

of almost entire small intestine, 800 cc creamy fluid aspirated, marsupialized (just managing to avoid intestinal walls), palpating finger reached to spine—interior of cyst smooth Recovery Microscopically, connective tissue, blood vessels, no endothelial or epithelial lining Author notes (1) Intestine and its lymphatics were entirely normal, (2) aspirated cysts refill, (3) drained (marsupialized) cysts heal

⁴ Braquehay, Jules Des Kystes du Mesentere Arch Gen de Med, 2, 291 and 572, 1892

A carefully written, comprehensive monograph covering historic, statistical, pathologic and clinical aspects to date Braquehay's statement—that Beneveni, the Florentine anatomist, was the first to observe a mesenteric cyst, in 1507—has been quoted ever since Fine bibliography, but misses a number of important early German references

⁵ Broca, A et Daniel, C Les kystes du mesentere dans l'enfance Rev de Gyn et de Chir abdominale, 9, 447, 1905

⁶ Carson, N B Chylous Cyst of Mesentery J A M A, 14, 674, 1890
Male, 39 Tumor size of a fetal head, between umbilicus and pelvis, diagnostic aspiration, chyle obtained Then three years elapsed Operation, five pints of chyle evacuated, marsupialization Recovery No description of operative findings, location of cyst, etc First American report of chyle cyst of mesentery

⁷ Collins, A N, and Berdez, G L Chyle Cysts of Mesentery Arch Surg, 28, 335, 1934

⁸ Crane, W Lymphangioma of Mesentery Am Jour Surg, 9, 441, 1930

⁹ Carter, R M Cysts of Mesentery Surg, Gynec, and Obstet, 33, 544, 1921

¹⁰ Dowd, Charles N Mesenteric Cysts ANNALS OF SURGERY, 32, 515, 1900

A comprehensive review to date Dowd (p 531) says " Chylous cysts are really preformed cysts situated in such close relation to the lacteals that chyle has been effused into them and that they are really embryonic in origin, in structure similar to ovarian and parovarian cysts "

This paper attracted wide attention, and with reason It was the first authoritative contribution on the subject in this country

¹¹ Ebhardt, K Beitrag zur Frage der Chyluszysten Buns Beitr z klin Chir, 156, 103, 1932

The most recent comprehensive monograph, it differs little, if any, with that of Henschen, in 1905 Both cover the subject thoroughly

Male, 3½ Entire abdomen filled by tumor Contrast roentgen ray studies of colon and kidneys proved them normal Cyst freed from great omentum and gas-

trocolic ligament and removed Opening in gastrocolic ligament sutured Recovery (An excellent line drawing accompanies this article)

Microscopically, marked predominance of lymph follicle formation in walls of polycystic lymphangioma (chylangioma), in contrast to lymph vessel hyperplasia in Godel's case Fluid not examined except to prove its sterility

- ¹² Eliason and North Perforated Chylous Cyst of Mesentery ANNALS OF SURGERY, 101, 1452, 1935

Marsupialized, recovered Microscopic examination of wall showed fibrous tissue with inflammatory changes, no differentiation of layers, no muscle fibers "Chylous cyst of mesodermal origin" Perforations previously reported by Pedersen (1) 1928 and Dutton (2) 1930 and Eliason (3) 1935

- ¹³ Elter, J Zur Retroperitonealen Cystenbildung Bruns Beitr z klin Chir, 30, 558, 1902

Male, 13 Epigastrium run over Celiotomy 14 days later Large retroperitoneal mass in left hypochondrium, gastrocolic omentum divided, 800 cc clear yellow fluid with some fibrin Marsupialized Recovery Cyst reached to vertebral column

Author gives a classification of retroperitoneal cysts, and lists previously reported retroperitoneal cysts (Rokitansky, Killian, Narath, Strehl, Sarwey, Enzmann, Obalinski, Zweifel, and Bardenheuer (The last two reported as retroperitoneal dermoids)

- ¹⁴ Enzmann Beitrage z path anat d Ductus Thoracicus Inaug Dissert, Basel, 1883
Female, 77 At autopsy Enzmann found what he considered a cyst of lower part of thoracic duct—greatly hypertrophied connective tissue walls Later authors fail to agree with this interpretation

- ¹⁵ Friend, E Mesenteric Chyle Cyst Surg, Gynec, and Obstet, 15, 1, 1912

- ¹⁶ Fatyol, C Operierte Falle (2) von Mesenterialer Chyluscysten Ztschr f Geburts u Gynak, 60, 1003, 1936

Case 1—Base of cyst (chyle cyst) broadly adherent to vertebral column and aorta, marsupialized

Case 2—Excised readily

Classification Ages vary from 4 mos to 71 yrs, male 1, female 4 Mentions involvement of plexus solaris ("synkope gefahr")

- ¹⁷ Gjorgjevic, V Uber Lymphorrhoe u Lymphangiome Arch f klin Chir, 12, 641, 1871

Excellent list of references, well written, interesting article by an assistant of Billroth's

- ¹⁸ Godel, Alfred Zur kenntnis der Peritoneal Zysten Frankfurter Ztschr f Path, 26, 564, 1921-1922

Male, 20, died of fractured skull Chance find at autopsy, polycystic (multilocular) chylangioma of mesentery of hepatic flexure Two parts, each the size of a child's head (1) Intraperitoneal, hung down into true pelvis (2) Retroperitoneal, behind ascending colon in angle between vertebral column, right kidney, and liver (An excellent illustration accompanies this article) Thoracic duct and cysterna chyli entirely normal Lymph nodes in the mesocolon, and wall of the colon itself entirely normal

The pathologic examination of the cysts of unusual interest The largest cyst, which seemed unilocular, proved to be multilocular on section Many solitary cysts of varying sizes also present The smaller isolated cysts were thin-walled, and contained a clear, fatty fluid All other cysts contained a milky fluid, which microscopically proved to be albuminous, with fat droplets and scattered lymphocytes Examination of the cyst walls showed large and small cystic, cavernous and simple telangiectatic regions, all close to each other, and all lined with a single layer of endothelium

Furthermore, the endothelial lining of cavernous and cystic, chyle-filled spaces

was surrounded by a definitely proliferating connective tissue stroma, localized to one part of the mesocolon, indicating a chylangioma, and with definite indications of new growth of lymph vessels through sproutings of endothelium, at first solid and later hollow. Godel also pointed out that the new growth of connective tissues was not present throughout the specimen, stating "We know that lymphangiomas have a tendency to become stationary and to undergo regressive changes, particularly cystic degeneration."

In all the larger cysts, there was a fibromuscular layer of varying thickness, forming projections into the lumen of the cyst cavity, and at the base of these projections, there was a rich capillary blood vessel network, besides, a whole system of lymph spaces communicated with the main cyst cavity.

In certain of the old thick-walled cysts, the endothelium had entirely disappeared. In these, the thick-walled connective tissue showed hyalin degeneration without elastic fibers, or smooth muscle. The endothelial lining had disappeared, there was calcified detritus. No signs of new growth of lymphatics, few blood vessels, and few lymph spaces. Round cell infiltration here and there.

Godel considers this to be a true tumor, a chylangioma of the mesocolon, a multicystic chylangioma.

Kayser, in 1914, was able to collect only 15 chylangiomas of the mesocolon, these were unilocular cysts, or occasionally multilocular solitary cysts. A case of multilocular polycystic chylangioma of the mesocolon could not be found in the literature at the time of Godel's publication.

The surgical aspect of this case was of interest, in that the intra-abdominal, pedunculated group of cysts could not have been completely excised, because at the base in the mesentery itself there was an infiltrating cavernous lymphangioma which had no sharp boundary. It is interesting to note that the young man had had indefinite abdominal complaints since early childhood.

Godel refers to the endless discussion as to whether these cysts are true new growths or are developed from varicosities of preformed lymph vessels, in other words, whether they are lymphangiomas or retention cysts. The difficulty lies in their rarity, and the incomplete and poorly described case reports.

There is a strong resemblance both macroscopically and microscopically between lymphangiectasis of normal lymph vessels, and true lymph vessel new growths. Besides all this, the two types may lie close to one another, and be actually in combination. For example, a tumor, originally a new growth, may come to a standstill and undergo marked changes through stasis. In order to prove that a given tumor is a lymphangioma, it is necessary to establish an actual new growth of lymph vessels, a condition rarely fulfilled among the few cases reported. The absence of such proof of new growth in adults is common. However, this absence is no proof against the cysts originating from a new growth to begin with.

¹⁹ Hadley, M. N. The Origin of Retroperitoneal Cystic Tumors. Surg, Gynec, and Obstet, 22, 174, 1916.

According to Hadley it seems more than probable that the group of abdominal tumors generally classed as chyle cysts do not all have the same origin. The only way we have of determining the nature of a cystic tumor is by a study of its life history, its location, the structure of its wall and the character of its contents. By these criteria, chyle cysts of the abdomen vary so widely that it seems hardly logical to ascribe a common mode of origin.

According to Florence Sabin, in the development of the lymphatic system there are two stages. First, the development of a series of isolated lymph sacs, which are clearly derived from the veins and which later become united by the thoracic duct which connects these sacs with each other. The second stage involves the peripheral growth of lymphatic vessels which sprout out from the endothelial lining to these sacs and spread over the body.

The process of development from the lymph sac to the adult lymph node is as follows. The lymphatic sacs by a process of bridging and cutting of the lumen by bands of connective tissue are transformed into a plexus of lymphatic capillaries out of which chains of lymph nodes are evolved. If this development of a particular lymph node was arrested at a stage when it was still a plexus, we would have the basis for the development of a future cyst. According to Hadley, it is some abnormality of the first stage of development in this primitive lymph sac that seems to offer the explanation of the origin of the retroperitoneal cystic tumors as well as those of the neck. The primitive lymph sacs are four in number. The jugular sacs located in the neck, the retroperitoneal sac located in the abdomen opposite the lower dorsal and upper lumbar vertebrae and the posterior sacs located in the pelvis. The retroperitoneal cystic tumors develop at a point corresponding in location to the primitive retroperitoneal lymph sac. Hadley concludes that the close similarity of neck and retroperitoneal lymph cysts seems strongly suggestive of a common origin. In addition, the fact that they arise where primitive lymph sacs originally occur is also strongly suggestive.

Abstract of Case Male, 48. Large abdominal tumor above and to the left of umbilicus. In March, 1911, family physician aspirated two quarts of milky, white fluid. Aspirations repeated September, December, 1911, and August, 1912, yielded 1½ gal yellowish fluid the color of chicken fat. At operation, August, 1912, enormous cystic tumor filled entire abdomen. The base rested against the posterior abdominal wall beneath the peritoneum extending from the arch to right of the vertebrae to within an inch of the left kidney. The tumor was easily enucleated. Uneventful convalescence until the 12th day, patient suddenly began to vomit and died two days later with symptoms of acute gastric dilatation.

"The tumor wall was fibrous, noncellular, and resembled connective tissue." There was no epithelium (endothelium) present on the inner wall. No chemical examination of contents made.

²⁰ Handfield-Jones, R. M. Retroperitoneal Cysts. Their Pathology, Diagnosis, and Treatment. Brit Jour Surg, 12, 119, 1924.

Defines retroperitoneal cysts as "those lying in retroperitoneal fatty tissues which have no apparent connections with any adult anatomic structure save by areolar tissue" (p. 120).

Again, lymphatic cysts are classified as (1) Those formed in the lymphatics returning from the intestine-chylous cysts. (2) Those arising in lymphatic field behind the peritoneum and not connected with the intestine—single cysts of varying size analogous in origin to single cystic lymphangiomas seen in the neck.

CLASSIFICATION OF RETROPERITONEAL CYSTS

Embryologico-Anatomic Basis

- | | | |
|---|---|---|
| (A) Cysts of urogenital origin | { | <ol style="list-style-type: none"> 1 Pronephric 2 Mesonephric 3 Metanephric 4 Mullerian |
| (B) Cysts of mesocolic origin | | |
| (C) Cysts arising in cell inclusions—teratomatous cysts | | |
| (D) Lymphatic cysts | | |
| (E) Traumatic blood cysts | | |
| (F) Parasitic cysts | | |
| (G) Cysts of developmental origin in fully formed organs—the kidney, the pancreas | | |

²¹ Hahn, Eugene. Über Mesenterial cysten. Beitr klin Wchnschr, 24, 408, 1887. Good summary.

²² Hedinger. Casuistische Beiträge z Kenntniss der Abdominalcysten. Virchows Arch 167, 29, 1902.

- ²³ Henschen, K. Beiträge z Geschwulstpathologie des Chylusgefäßsystems. Inaug. Dissert., Zurich, 1905

The most comprehensive monograph on the subject up to the present. All aspects of the subject are covered. Excellent list of references (252). For the reader's convenience, the following summarized excerpts may be of interest. Henschen states that the presence of chyle-like fluid may come from relatively few connections with chyle-bearing lymphatics or may come through fatty degeneration of tissue lining the cysts. Henschen (p. 66 and 67) refers to Koblanck and Pfoite's case (Virchows Arch., 161, 44, 1900), of a woman, age 61, with a huge retroperitoneal cyst containing 25 liters of creamy fluid identical in its chemistry and morphology with those of chyle, yet microscopic examination proved it to be a huge hydro-nephrosis.

Again (p. 70 and 71). In the starving animal, chyle and lymph are practically the same. The amount of fat found in chyle depends upon quantity and quality of ingested food. Henschen quotes the following observations to show that lymph in lymphatics (of the extremities, for example) after fatty meals, contains fat in practically the same percentages as that in the chyle-bearing lymphatics. Thus, Hensen (Pflügers Arch., vol. 10) in a boy of 10, with a lymph fistula, reported from 28 to 39.6 per cent of fat in lymph. Lang (after Hammersten, text-book of physiologic chemistry, 3rd ed., 1895, p. 159), in a girl of 17, with a lymph fistula of thigh, an average of 24.5 per cent fat in lymph, lastly, Munck and Rosenstein (Virchows Arch., vol. 123), in a girl of 18, weighing 60 Kg, found 0.6 to 2.6 per cent fat during hunger periods rising to 47 per cent after fatty meals.

- ²⁴ Hensen. Über die Zusammensetzung einer als Chylus aufzufassenden Entleerung aus der Lymphfistel eines Knaben. Arch. f. d. ges. Physiol. v. Pflüger, 10, 94, 1875.

- ²⁵ Higgins, T. T., and Lloyd, E. 1924, (Slocum) Mesenteric Cysts with Report of Two Cases. Brit. Jour. Surg., 12, 95-105, 1924.

Male, 5. Tumor occupied entire right side of the abdomen. "X-rays demonstrated a retroperitoneal tumor pushing intestines forward." Celiotomy. Multilocular cyst, 35 oz. brown, turbid, odorless fluid, thick wall of fibrous tissue with endothelial lining. (An excellent illustration accompanies this article.)

Female, 45. Cyst, right lumbar and right hypochondriac regions. Right lumbar incision. Seven pints greenish-brown fluid, aspirated. Excision. Recovery.

- ²⁶ Hill, J. M. Mesenteric Chyladenectasis. Am. Jour. Path., 13, 267-276, 1937. Discussion and bibliography.

- ²⁷ Hochenegg. Lymphcyste d. Mesent. Wien. klin. Rundsch., 81, 1895.

- ²⁸ Hoffmann, V. Zur Kenntnis der Chyluscysten. Deutsch. Ztschr. f. Chir., 151, 137-142, 1919.

- ²⁹ Heuper, W. Mesenteric Enterocystomata. Jour. Lab. and Clin. Med., 12, 427, 1926.

- ³⁰ von Hippel. Retroperitoneale Lymphcyste und Pankreascyste. Arch. f. klin. Chir., 88, 1014, 1909.

Female, 63. Large retroperitoneal cyst—gallbladder above, stomach and first part of duodenum displaced downwards (they lie on mesial and anterior aspects of cyst wall), transverse colon below, right kidney outside and behind. Unilocular, three extensions toward vertebral column—one strand extending mesially and backward, joins another from above, 3 cm. away from cyst wall (in Strauss and Sayre's case, cyst wall was smaller—has similar strands. Schorlemmer's case likewise—Author). These extensions contained chyle, ligated and divided. Marsupialization. Death 28 days later from large abscess in pouch of Douglas, secondary to old ischio-rectal abscess. No connection with cyst. At postmortem, cyst wall found adherent to duodenum and colon, separate from pancreas. Right kidney free from cyst, but had two orange-sized cysts of its own. Tracts described at operation not found at hurried autopsy.

- ³¹ Killian, G Eine grosse retroperitoneale Cyste mit Chylusartigen Inhalt Berlin klin Wchnschr, 23, 407, 1886
Female, 61 Tumor in right hypochondrium, aspirated twice, 2,500 cc and again four weeks later, 2,200 cc obtained Operation four weeks later Celiotomy—Marsupialization Hand introduced into open cyst could feel the psoas, vertebral column and aorta to left, right kidney lay in front of cyst wall Recovery Specimen of wall not taken (Probably the first case to be operated upon in Germany)
- ³² Klemm, Paul Beitrag zur Genese der Mesent Chylangiome Virchows Arch, 181, 541, 1905
Male, 2½ Multilocular chyle cyst of mesentery of ileum Small intestine (ileum) stretched like a flat band over cyst wall Resection, recovery Cyst contained 1,500 cc of chyle Specimen showed dilated tortuous lymphatic vessels for 25 to 30 cm from cyst wall Close to the cyst, cavernous formation
Discusses variations in
Site from radix to edge of intestine, usually in mesentery of small intestine (50) rarely in mesocolon (2)
Size Microscopic, to that of a cocoanut or larger
Number 1 Single unilocular the most frequent
2 Less frequently multilocular unicystic or polycystic
3 Or variations, viz, one large, many smaller (see Tuffier)
Good, detailed microscopic description of cyst wall For cases similar to Klemm's see Ritter (after Klemm), Moynihan, and Vertan
- ³³ Koblanck and Pforte Hydronephrose mit chylusahnlichem Inhalt und eigenartiger Wand, nebst Bemerkungen uber Chyluscysten Virchows Arch, 161, 44, 1900
Woman, 61 A huge retroperitoneal cyst containing 25 liters of fluid identical in its chemical and morphologic constituents with those observed in chyle Microscopic examination of elements of cyst wall proved it to be a hydronephrotic sac
- ³⁴ Lanzarini A Large Cystic Lymphangioma of the Right Iliac Fossa (transl) Zentralbl f d Gesamte Chir, etc, 4, 714, 1914
Female, 49 Excision Microscopic Multiple lymphangiomata
- ³⁵ Millard and Tillaux Kyste due mesentere chez un homme Bull Acad de Med de Paris, 17, 831, August, 1880
Male, 31 Tillaux (Operator) Celiotomy—Pedunculated chyle cyst of the mesentery Excision Was "like removal of an ovarian cyst" (Early French case)
- ³⁶ Minnervini, R Lymphangioma of the Omentum, Multiple Cystic Lymphangioma of the Abdomen La Clinica Chirurgica, 23, 90, 1915
- ³⁷ Moynihan, B Tumors of the Mesentery Med Chron, 36, 345, 1902 See also ANNALS OF SURGERY, 26, 1-30, 1897 (Moynihan's case similar to Klemm's and Vertan's)
- ³⁸ Most, A Chirurgie der Lymphgefasse und der Lymphdrusen Neue Deutsche Chirurgie, 24, 307, 1917
Brief but comprehensive Very worthwhile
- ³⁹ Narath, A Uber retroperitoneale Lymphcysten Arch f klin Chir, 50, 763, 1895
(1) Male, 52 Cyst size of man's head occupied left half of abdomen Drained by left lumbar incision, 4,000 cc of chyle obtained Death from sepsis Postmortem Wall 1 Mm thick, cyst in front of left kidney Considered to have originated in left lumbar lymphatic plexus No microscopic examination of cyst wall
(2) Female, 22 Large retroperitoneal cyst the size of a man's fist, pointing in thigh At operation (excision) found to originate near transverse process of lumbar vertebra two fingersbreadth below umbilicus Unilocular with several extensions Wall thin in some places, thicker in others Lining Granulation tissue with foreign body giant cells
Strehl (Deutsch Ztschr f Chir, 178, 1899) and Minssen (Deutsch Ztschr f

Chur, 83, 577) questions whether Narath's second case was not that of a psoas abscess

⁴⁰ Obalinski, A. *Über seröse retroperitoneale cysten*. *Wien klin Wchnschr*, 4, 719, 1891

Female, 57. Cyst size of man's head. Diagnosed as hydronephrosis or echinococcus cyst, was retroperitoneal in right lumbar region, aspirated, then enucleated easily. Microscopic examination of wall, fibrous connective tissue and elastic tissue. Contents Watery. Apparently a retroperitoneal lymph cyst from müllerian or wolffian tests. (Przewoski, Polish author, 1889)

Obalinski lists cases of serous cysts prior to 1891, Bramann, Hahn, Solman, Kosinski

⁴¹ Proust and Monod. *Contribution to Study of Mesenteric Cyst Especially Chyle Cysts*. *Rev de Gynec, etc*, 19, 225, 1912

A comprehensive monograph, detailed reports, good illustrations, very complete reference list

⁴² Prutz, W., and Monnier, E. *Die Chirurgischen Krankheiten u die Verletzungen des Darmmerkreises und der Netze*. *Deutsche Chirurgie*, 46, 1913

Chapter on cysts and tumors of the mesentery (especially p 338-343) gives a brief but comprehensive summary on lymphangiomata. Also includes Henschen's classification of mesenteric cysts—analogueous to Handfield-Jones classification of retroperitoneal cysts

⁴³ Quincke, H. *Deutsch Arch f klin Med*, 16, 121, 1875

Describes chylous ascites—due to cicatricial obstruction to lacteals of mesentery close to border of intestine, also obstruction of thoracic duct by tumor growth, with rupture of distended lacteals. Lastly, rupture of thoracic duct by whooping cough paroxysms followed by chylous ascites. (Wilhelms)

⁴⁴ Ribbert, H. *Virchows Arch*, 151, 381, *Geschwulstlehre*, 151, 181, 1904, *Allgemeine Pathologie*, p 223-224 and 249

⁴⁵ v Ritter (Chiari's pupil in Prague). *Zur Kenntniss der Cystischen Lymphangiome in Mesenterium des Menschen*. *Ztschr f Heilk*, 21, 31, 1900

⁴⁶ Roller, C. S. *Mesenteric Cysts*. *Surg, Gynec, and Obstet*, 60, 1128, 1935

Good historic review. Estimates 500 cases in the literature. Interesting statistics from recent hospital reports showing great rarity of the condition. (See Slocum also)

⁴⁷ Rosenheim. *Demonstration eines Präparates von Multilocularen chylosen Mesenterialcysten b Kinde*. *Deutsch med Wchnschr*, 23, 68, 1897

⁴⁸ Rokitansky. *Lehrbuch d Path Anat*, 3 Aufl, 2 Teil, p 295 (after Elter)

Postmortem. Male, 36, Pulmonary tuberculosis. Retroperitoneal cyst size of a child's head. Pancreas above, duodenum to right, descending colon to left. Contents Milky fluid, blood tinged. Varix-like enlargement of a lumbar extension

⁴⁹ Sarwey, O. *Ein Fall von retroperitonealer chyluscyste bei einem 11 jährigen Mädchen*, *Exstirpation, Heilung*. *Centralbl f Gyn*, 221, 407, 1898

Female, 9. First seen August, 1894. Two years previously abdominal tumor noticed. Two aspirations made previously, in September, 1893, and in June, 1894. Admitted to the clinic December, 1894, to August, 1895. In May, 1895, tumor aspirated, 6,200 cc clear, milky fluid drawn off. Second admission December 20, 1895. Aspiration March, 1896, 6,000 cc obtained. (Note. In 1896, child fell striking abdomen, was sick with symptoms of peritonitis for three weeks in bed.) Discharged August, 1897. November, 1897 (third admission)

Celiotomy December 3, 1897. Huge retroperitoneal tumor. Posterior parietal peritoneum divided in order to expose cyst. Cyst opened and five liters of same typical milky fluid obtained. The stem of cyst projected from between stomach and transverse colon and originated from posterior parietes. (An excellent line drawing accompanies this article.) Was easy to trace stem of cyst to head of pancreas with which it was connected by a stem 2 cm long, the thickness of a little finger. Here

it was divided, and the same milky fluid escaped from the proximal end. No adhesions with any of the neighboring organs. Stump cauterized with actual cautery, buried and abdomen closed. Uneventful convalescence.

Chemical and microscopic examination of contents showed similarity to milk, no digestive ferments. *Cyst Wall* Uniformly smooth interior except on a few spots where there are smaller daughter cysts. Microscopic examination showed smooth muscle cells, connective tissue, blood vessels, endothelial lining. *Diagnosis* Retroperitoneal unilocular chylangioma. (At time of extirpation the girl was 11 years old.) A good review of subject up to date of publication.

- ⁵⁰ Sick, Conrad. Beitrag zur Bau u Wachstum der Lymphangiome. Virchows Arch, 170, 9, 1902

Male, 21. Retroperitoneal cavernous lymphangioma with cyst formation involving most of the retroperitoneal space from diaphragm to pelvis and to both sides of the vertebral column. Detailed pathologic report clearly illustrated. Well worth reading in original. A good example of a misleading title—no one could guess it to indicate a *retroperitoneal* lymphangioma.

A tumor of this extent and character is inoperable.

- ⁵¹ Schorlemmer, R. Beitrag zur casuistik der retroperitonealen cysten. Deutsch med Wchnschr, 28, 914, 1902

Male, 54. For six months some difficulty in swallowing, stomach trouble, belching. Noticed a tumor of the right side of abdomen below naval near midline. Operation—Feb 17, 1902. Cyst to the right, retroperitoneal, unilocular, contained about 1,000 cc of chyle. Upper and lower poles impossible to remove. These were ligated and remainder of cyst excised. No connection with pancreas or lymph nodes. Posterior parietal peritonium sutured. Recovery. Microscopic examination of cyst wall. Connective tissue with a tendency to fatty degeneration of the layers from without inwards. No endothelial or epithelial lining. (Absence of endothelial lining noted by most authors.) In fluid—fat droplets, no pancreatic ferments. Schorlemmer considers the preoperative belching and dysphagia to have a reflex irritation as their cause. (Patient admitted lifting a very heavy wagon.)

- ⁵² Slocum, M. A. Surgical Treatment of a Chylous Mesenteric Cyst by Marsupialization. Am Jour Surg, 41, 464, 1938

Female, 48. Cyst filled almost entire left upper quadrant of abdomen, size reduced by aspiration (1,000 cc), cyst opened, aorta and vertebral column to be felt through cyst wall. One loop of small intestine densely adherent to cyst. Recovery. Cyst wall showed connective tissue, lymphocytes, no endothelial lining. *Diagnosis* Chyle cyst of mesentery with fibrosis and chronic inflammation. Analyses of chyle similar to those cited by Henschen (1905).

- ⁵³ Smoler, F. Zur Kasuistik der Mesenterialen Lymphcysten. Bruns Beitr z klin Chir, 32, 295, 1901-1902

Male, 60. Chyle cyst in mesentery of small intestine size of a child's head. Radiating, distended lymphatics contained chyle. Cyst aspirated first to lessen its size then enucleated (it reached to root of mesentery). Cyst wall 2-4 Mm thick. Accurate gross and microscopic description of three separate layers of cyst wall.

Smoler notes that presence and absence of endothelial lining of cyst wall is reported by equal numbers of authors. In all cases, however, endothelium is seen lining lymph spaces within cyst wall proper.

- ⁵⁴ Speckert, J. Ein Fall von Chyluscyste. Arch f klin Chir, 75, 998, 1905

Female, 29. Chyle cyst in mesentery of lower ileum, marsupialized. Recovery. Well two and one-half years later. Detailed microscopic description of three layers of cyst wall.

A carefully written, comprehensive article, covers historic, pathologic and clinical aspects, including differential diagnosis treated in considerable detail.

It is interesting to note meticulous description of the physical examinations of that era. They included examination under anesthesia, with patient in Trendelenburg

position, and pelvic examination as a matter of course, also inflation of stomach and of colon to determine relation of cyst (or tumor) to the intestines and to the liver, measures less frequently resorted to since advent of roentgenologic examination

- ⁵⁵ Strauss, S F, and Sayre, B E Retroperitoneal Chyle Cyst ANNALS OF SURGERY 102, 1118, 1935

Female, 38 Retroperitoneal chyle cyst size of a grapefruit, liver and gall-bladder upwards and to right, stomach and duodenum below and to left Posterior parietal peritoneum incised Three large lymph vessels seen going into anterior surface—upward, downward and to the left Ligated Cyst removed Cyst bed drained No subsequent leak of chyle Recovery Fluid “Chyle, verified by microscopic examination” No report on cyst wall

- ⁵⁶ Strehl, Hans Retroperitoneale lymphcyste oder senkungsabscess Deutsch Ztschr f Chir, 51, 178, 1899 Assistant to Eiselsberg in Königsberg

Cites Narath's case of the 22 year old girl and considers it probably of tuberculous character with clear fluid content His own case (1897), man of 20 operated upon by von Eiselsberg, was considered to closely resemble Narath's case Portion of cyst present in thigh (left) was incised and one liter of clear yellow fluid escaped Interior of cyst wall showed many polypoid excrescences Finger introduced through this opening in thigh passed upwards beneath Poupart's ligament into pelvis A sound could be passed upwards to the region of the left kidney Part of cyst wall removed for microscopic examination Many giant cells in wall and in certain places typical miliary tubercles Therefore Strehl is certain this was a tuberculous abscess pointing in the thigh, although no bony focus could be demonstrated (König speaks of “congestionsabscessen” with serous contents, ref Textbook for Special Surgery, Vol 3, p 374) Strehl considers the fact that the so-called cyst could not be readily enucleated but was densely adherent to fascia and intramuscular ligaments as additional evidence for the diagnosis of tuberculosis

In Strehl's case, the cavity was filled with iodoform glycerin and the wound was closed tightly Nevertheless, the wound broke down and a fistula developed which seemed to be closing at the time of publication

- ⁵⁷ Swartley, W B Mesenteric Cysts ANNALS OF SURGERY, 85, 86, 1927

Abstract Rokitsansky, Brucy and Virchow ascribed origin from degenerated lymph nodes Dowd, in 1900, reported a cyst of transverse mesocolon in a woman, closely resembling a multilocular ovarian cyst He suggested its originating from embryonic sequestration Moynihan and Ayers also stressed embryonic origin Klemm considered cysts as neoplasms developing from misplaced or sequestered portions of mesodermic tissue, *ie*, embryonic in origin Cystic disease of the mesentery is more frequent in women than in men

First case Female, 7 Cyst, mesentery of ileum size of grapefruit Wall showed three layers—inner, serous, middle, muscular, and a thick fibrous envelope undergoing calcareous changes

Second case Male, 26 History of trauma in region of right kidney Cyst in mesentery of upper jejunum Enucleation Recovery Contents “Sebaceous material”

- ⁵⁸ Syme, Parker Chyle Cysts of Mesentery ANNALS OF SURGERY, 23, 605, 1896

Male, 19 Cyst in mesentery of ileum, four inches in diameter, “14 oz pure chyle”, enucleated, recovery

- ⁵⁹ Tilger, A Über ein Fall von Lymphcyste innerhalb des Ligamentum Hepatogastricum Virchows Arch, 139, 288, 1895

Postmortem Female, 71 Died of uremia and bronchopneumonia Healed gastric ulcer at lesser curvature, unilocular lymph cyst containing 14 cc of yellowish, fatty fluid in gastrohepatic ligament

Tilger's concept of a “lymphangitis chronica desquamativa” as causing this cystic formation did not meet with acceptance by later authors To sustain his contention Tilger cited the report of Engel Reimers (Arch f klin Chir, 23, 632, 1879) of a

lymphangioma of the stomach wall supposedly due to stenosis of lymph vessels following cicatricial contracture of a chronic gastric ulcer of the lesser curvature (Obviously cases of coincidence—not of cause and effect [Author])

⁶⁰ Timbal, R. *Rev de Chir*, 41, 45, 1910. Early, frequently quoted article

⁶¹ Tuffier. Unilocular Chyle Cyst of the Mesentery (Small Intestine) *Bull et Mem de la Soc de Chir de Paris*, 18, 582, 1892, and 30, 457, 1904

Case 1—Male, 48. Size of head of a fetus, in the mesentery close to vertebral origin. Excised, cured. 600 cc of fluid in cyst.

Case 2—Child, 12. Signs of chronic intestinal obstruction for several years. Multilocular. One cyst contained one liter of serous fluid, another, two liters of chylous fluid. Many numerous small cysts infiltrated the mesentery.

⁶² Vertan, E. *Über ein seltenen Fall von Chylangioma cysticum Mesenterii*. *Zentralbl f Chir*, 63, 86, 1936

Female, 5. Operated for chronic appendicitis, at celiotomy—free milky fluid present. Two mesenteric cysts of ileum pinched the intestine between them, 10 cm of intestine resected with cysts. End-to-end suture. Recovery.

Good illustration. Klemm, Moynihan also had similar cases.

⁶³ Volkmann, J. *Über chylus cysten am Halse*. *Bruns Beiträge z klin Chir*, 146, 654, 1929

Male, 34. Fluctuating swelling, size of a hen's egg, in right supraclavicular region. Diagnosis lay between cold abscess, bronchial cyst and lymph cyst. At operation, cyst was easy to enucleate except where densely adherent to internal jugular vein which was injured but repaired. Several enlarged lymphatic vessels seen leading into cyst. Multiple fine ligatures to cyst bed, it being impossible to pick up individual lymph vessels. Recovery.

Cyst unilocular, smooth inner wall. Microscopically, the wall showed three layers. Outer. Thin vascular connective tissue, with much perivascular infiltration. Middle. Dense connective tissue, with many circular elastic fibers and few smooth muscle fibers, containing many widened lymph capillaries. Inner. Longitudinal elastic fibers, with a single layer of endothelial cells lining the inner aspect. This intima coat showed scattered round cells. A few lymph follicles in the wall at one point. Diagnosis "Lymphangioma chylocysticum, partim cavernosum."

Volkmann gives nine references regarding chyloorrhea of the lower extremity (See Henschen²³ also). There is an extensive tabulation of the chyle obtained from his own three cases, and compared with that obtained by Grauhan (Grauhan's case was in a pregnant woman, and the fluid might have come from an aberrant mammary gland.)

The author considers the embryology of lymph vessel formation according to Bonnet (See Handfield-Jones,²⁰ Florence Sabin's work), and cites Herbert Neumann's etiologic classification of tumors of the lymphatic vessels (*Arch f klin Chir*, 147, 314, 1927.)

(1) Mechanical Theories

(A) Distention of the afferent lymph vessels of thoracic duct, caused by tumors, congenital defects, infarct of inspissated chyle, obliteration of the main duct

(B) Trauma

(a) Traumatic escape of lymph

(b) Rupture of the thoracic duct

(C) Chronic inflammation of lymph nodes in tuberculosis, typhoid fever, dysentery

(a) Inflammatory changes in the node itself, or,

(b) In the afferent lymph vessels, through independent growth of the wall

(2) Neoplastic Theories

(A) Congenital (chylangioma of Henschen)

(B) From the mesoderm

- ⁶⁴ Warfield, J O A Study of Mesenteric Cysts with Report of Two Cases ANNALS OF SURGERY, 96, 329, 1932

Study of 129 cases of mesenteric cysts (estimates 500 in the literature) Extensive bibliography on both mesenteric tumors and cysts

- ⁶⁵ Wegner Uber Lymphangioma Langenbeck's Arch f klin Chir, 20, 641, 1877

Was the first to classify (differentiate) lymphangiomata as simple, cavernous and cystic His classification accepted ever since

- ⁶⁶ Weichselbaum Eine seltene Geschwulstform des Mesent (Chylangioma cavernosum) Virchows Arch 64, 145, 1875

Male, 80 Died of scurvy and pneumonia Chance finding at postmortem Tumor of mesentery of upper ileum size of a saucer, at first taken for a lipoma—proved, microscopically, to be a fatty, cavernous lymphangioma showing all stages simplex, cavernous and cystic forms (See also cases of Smoler, Klemm, and Godel) One of the first cases to receive detailed microscopic study

Weichselbaum refers to Billroth (1858), who held that activity of the connective tissue stroma was responsible for originating the process in lymphadenoma cavernosum Weichselbaum questioned how chyle could occur in lymphadenomata so far from the lacteals Cited Desjardins (1854), a woman with a lymphadenoma simplex of thigh and abdominal wall, leaking milky fluid, fat droplets, etc Aubry (1866) found milky fluid in cysts of thigh Petters (1875) found milky fluid in a labium majus (See also reference to Henschen above) Weichselbaum noted fatty degeneration of endothelium and inner walls of cyst

- ⁶⁷ v Winiwarter, A Chylangioma Cavernosum in Abdomine Med-Chir Centralblatt (Wien), 14, 4 and 15, 1879

Female, age 4 months Born with abdominal mass, now so enlarged that respiratory and alimentary functions were impeded Aspirations of milky fluid from left hypogastrium as follows (1) April 20, 1876, 3,000 cc, (2) September 12, 1876, (3) November 18, 1876, (4) December 19, 1876, (5) January 16, 1877, 2,000-3,000 cc each time The parents then decided against operation and the patient was lost track of

DISCUSSION—DR ALLEN O WHIPPLE (New York) discussed the differential diagnosis of retroperitoneal chyle cysts and of retroperitoneal cysts and tumors in general, because of the difficulties they present in accurate diagnosis, which has so much to do with accurate and efficient surgical therapy He also discussed certain points in regard to the operative therapy of intra-abdominal cysts, particularly the retroperitoneal varieties

In regard to differential diagnosis, Doctor Whipple pointed out that these masses appear on both the right and left sides and, on the right side, have to be differentiated from enlargements and tumors of the gallbladder, duodenum, adrenals, kidney, liver and pancreas Accurate roentgenologic studies, with cholecystograms, barium studies of the duodenum and jejunum in relation to the palpable mass, and pyelograms, both intravenous and retrograde, help tremendously in reaching a diagnosis, as was well illustrated in Doctor Geister's case

On the left side, these masses have to be differentiated from stomach, spleen and pancreas, left adrenal and left kidney Perhaps the most frequently overlooked lesions are the tumors of the stomach, which can be very easily confused with cysts of the pancreas and with enlarged spleens In these left-sided masses, a small amount of barium by mouth together with a barium enema help greatly in determining the relation of the cyst to the stomach and bowel Accurate urologic studies are also very important At times an ordinary roentgenogram of the abdomen shows a calcification of the wall in these cysts which frequently narrows the diagnosis to a pancreatic or renal cyst Sometimes a pneumoperitoneum will give accurate information Doctor Whipple said he

was not familiar enough with the peritoneoscope to say whether or not this examination would be of real help

Concerning operative therapy, excision is the procedure of choice and gives, without question, the best results. But in so many of these retroperitoneal cysts, especially those connected with the pancreas, as well as the dermoid cysts, retroperitoneal excision is exceedingly difficult. At times excision can be accomplished in two stages, if a one-stage procedure is not possible, *i e*, after partial excision and marsupialization, or the shrinking of the cyst and its surrounding vessels, the remains of the cyst can be removed by a second operation. Doctor Whipple said he had done this in two cases where it was impossible to consider excision.

Other possible procedures are partial excision with marsupialization, marsupialization, when it is the only method possible, with the employment later of a sclerosing solution, for the deep-seated cysts, drainage, and later the injection of sclerosing fluid, and anastomosis of the cyst wall to the stomach or the jejunum, as has been done in several instances of pancreatic cysts. Doctor Whipple said he had performed an anastomosis between the cyst and the stomach in a case of cyst of the pancreas.

DR THOMAS H RUSSELL (New York) described two cases of mesenteric cyst which he had recently encountered. One followed trauma. It was a compensation case about which Doctor Russell stated in his report to the insurance company that he did not know whether trauma had anything to do with it or not. The company took it for granted that it was due to trauma and settled. The cyst was the size of a small orange and was freely movable. The patient had both kidneys of the wandering type, particularly on the left side, and Doctor Russell took the cyst to be a left kidney. He approached it through a loin incision but the kidney did not have the degree of mobility he expected. He delivered a large cyst which he was able to dissect free from the mesentery. The patient's chief complaint was pain in the back, which Doctor Russell had attributed to the kidneys rather than to a cyst. The patient was entirely relieved.

The second case occurred in a man, in the sixties, who had had his leg amputated for an epithelioma of the foot that would not heal. He had a mass that could be shifted all around the right side of the abdomen. The chief complaints were obstruction and clamp-like pains. Shortly after being discharged from the hospital following the amputation of his leg, he was readmitted for intestinal obstruction. The roentgenographic report was that of a mass, possibly a neoplasm of the sigmoid. Doctor Eggeis was prepared to operate when the mass suddenly disappeared. The patient was discharged, but returned several weeks later with a recurrence of the mass. Doctor Russell opened the abdomen and found a cyst involving the lower part of the ileum and sigmoid only. An ileotransverse colostomy was performed because the man's condition was not very good, intending later to remove it. The cyst seemed to be in the wall of the cecum and produced obstruction. The ileum was markedly dilated. After the patient left the operating room he ceased to breathe for one hour and 15 minutes, during all of which time Doctor Peterson treated him by artificial respiration. The patient recovered. The cyst again disappeared, and he was discharged. The second-stage operation has not yet been undertaken.

DR JOHN C A GERSTER (closing) recalled that sclerosing solutions after marsupialization were much in vogue in the early cases. Modern solutions are more effective and less dangerous. He called attention to the fact that Doctor Russell's cases were both of *mesenteric* chyle cysts, of which there are 450 to 500 reported in the literature. A most careful search has failed to disclose more than 16 to 18 *retroperitoneal* chyle cysts. The scope of the paper did not permit consideration of *mesenteric* chyle cysts.

THE RÔLE OF THE NERVOUS SYSTEM IN ACUTE INTESTINAL OBSTRUCTION

AN EXPERIMENTAL INVESTIGATION

JACOB FINE, M D , LOUIS ROSENFELD, M D , AND SAMUEL GENDEL, M D
BOSTON, MASS

FROM THE SURGICAL LABORATORIES, BETH ISRAEL HOSPITAL, AND THE DEPARTMENT OF SURGERY, HARVARD MEDICAL
SCHOOL, BOSTON, MASS

AMONG the numerous factors which have been considered significant in the death from acute intestinal obstruction, the nervous system has been alluded to recently by Herin and Meek¹ and by Taylor, Weld and Harrison². These investigators claim to have prolonged the survival time of dogs, dying from distention of intestinal loops, by denervation of the adjoining mesentery. The renewed impetus recently given to the nervous element in traumatic shock (O'Shaughnessy,³ Freeman⁴), to which the prelethal stage of intestinal obstruction has been compared (Moon⁵), perhaps adds weight to the need of further appraisal of this aspect of the condition. An experimental technic, which we believe permits a more crucial evaluation of the adverse effects of nervous stimulation in acute intestinal distention than is possible by the method of Herin and Meek or of Taylor, Weld and Harrison, was utilized in the work which forms the basis of this communication.

METHOD EMPLOYED—The celiac ganglion and all the splanchnic nerves or the subdiaphragmatic vagus nerves, or both, were resected in the cat. (The adequacy of the resection was confirmed by postmortem examination in all instances.) Several days or weeks later, when the animal was fully recovered, the *empty* small intestine (*i.e.*, the cat had been allowed only water for the preceding 24 hours) was ligated, under ether anesthesia, at the pylorus and the ileocecal valve and a glass cannula leading from a Perusse bottle tied securely into the terminal ileum. The abdomen was closed around the cannula and the animal allowed to recover from the anesthetic. The entire small intestine was then inflated with air which was maintained at a constant intraluminal pressure. The level of pressure, which varied in different groups of animals from 100 to 800 Mm of water pressure, was established gradually by increasing increments of 100 Mm of pressure every hour. At the termination of the experiment upon the death of the animal, the survival time, the fluid content of the stomach, intestine and peritoneal cavity and the condition of the bowel wall were observed (37 experiments) and compared with corresponding control animals which had not been denervated (25 experiments) and other control animals which were neither distended nor denervated (6 experiments).

Five of a series of 10 dogs were subjected to spinal cord transection at the fourth to the fifth dorsal segment. Three to five days later, without further denervation, they were distended in the same manner as the cats. The same

TABLE I
TOTAL FLUID CONTENT OF SMALL INTESTINE IN CUBIC CENTIMETERS

		100Mm H ₂ O Pressure			200Mm H ₂ O Pressure			400Mm H ₂ O Pressure			600Mm H ₂ O Pressure			800Mm H ₂ O Pressure		
Normal Cats	Obstruction Without Distention	—Denervation—			—Denervation—			—Denervation—			—Denervation—			—Denervation—		
		Control	Celiac Resection	Celiac and Vagotomy	Control	Celiac Resection	Celiac and Vagotomy	Control	Celiac Resection	Celiac and Vagotomy	Control	Celiac Resection	Celiac and Vagotomy	Control	Celiac Resection	Celiac and Vagotomy
1	90	34	56	63	—	88	99	62	24	29	78	38	57	21	26	—
2	45	18	27	—	—	34	43	70	41	27	65	57	28	30	55	—
3	58	24	40	—	—	36	40	41	13	18	49	30	30	41	10	—
4	23	—	—	—	—	98	110	31	15	30	62	45	45	8	9	—
5	12	—	—	—	—	28	38	—	—	—	40	—	—	20	—	—
6	—	—	—	—	—	18	24	—	—	—	—	—	—	—	—	—
7	—	—	—	—	—	14	28	—	—	—	—	—	—	—	—	—
Av	9	46	25	41	63	45	49	51	23	26	59	48	40	31	41	—
Group Av	9	46	25	43	1	45	41	9	—	26	43	0	—	31	35	6

		PERITONEAL FLUID		
1	2	13	24	31
2	1	34	3	—
3	7	16	7	—
4	14	—	—	—
5	—	—	—	—
6	—	—	—	—
7	—	—	—	—
Av	5	21	11	—
Group Av	5	21	16	1

		SMALL BOWEL WEIGHT AS PER CENT OF BODY WEIGHT											
1	1 61	2 08	2 04	3 10	2 75	1 66	1 60	2 25	1 57	2 57	2 70	1 21	2 00
2	2 86	1 88	2 77	1 51	—	2 18	2 49	2 29	2 11	3 83	2 20	3 28	2 39
3	2 71	3 10	2 10	2 21	—	1 77	2 37	2 21	2 04	2 77	1 33	1 72	1 72
4	3 14	1 58	—	—	—	2 33	2 23	—	—	—	—	—	—
5	1 61	—	—	—	—	2 50	—	—	—	—	—	—	—
6	2 86	—	—	—	—	2 58	—	—	—	—	—	—	—
7	2 71	—	—	—	—	2 25	—	—	—	—	—	—	—
8	1 92	—	—	—	—	2 48	—	—	—	—	—	—	—
Av	2 13	2 16	2 30	2 27	2 75	1 99	2 31	2 25	2 09	3 06	2 27	2 24	2 37
Group Av	2 43	2 16	2 30	2 44	—	1 99	2 16	—	—	—	—	—	—

INTESTINAL OBSTRUCTION

data were obtained from these animals as from the cats and compared with those from five other dogs which were neither deneivated nor had their spinal cords transected

RESULTS —(A) *Effect of Deneivation on Survival Time* In Chart 1 the survival times of the various groups of cats have been plotted against the levels of intra-intestinal pressure. From these data it appears (1) That the survival time is inversely proportional to the height of the intra-intestinal pres-

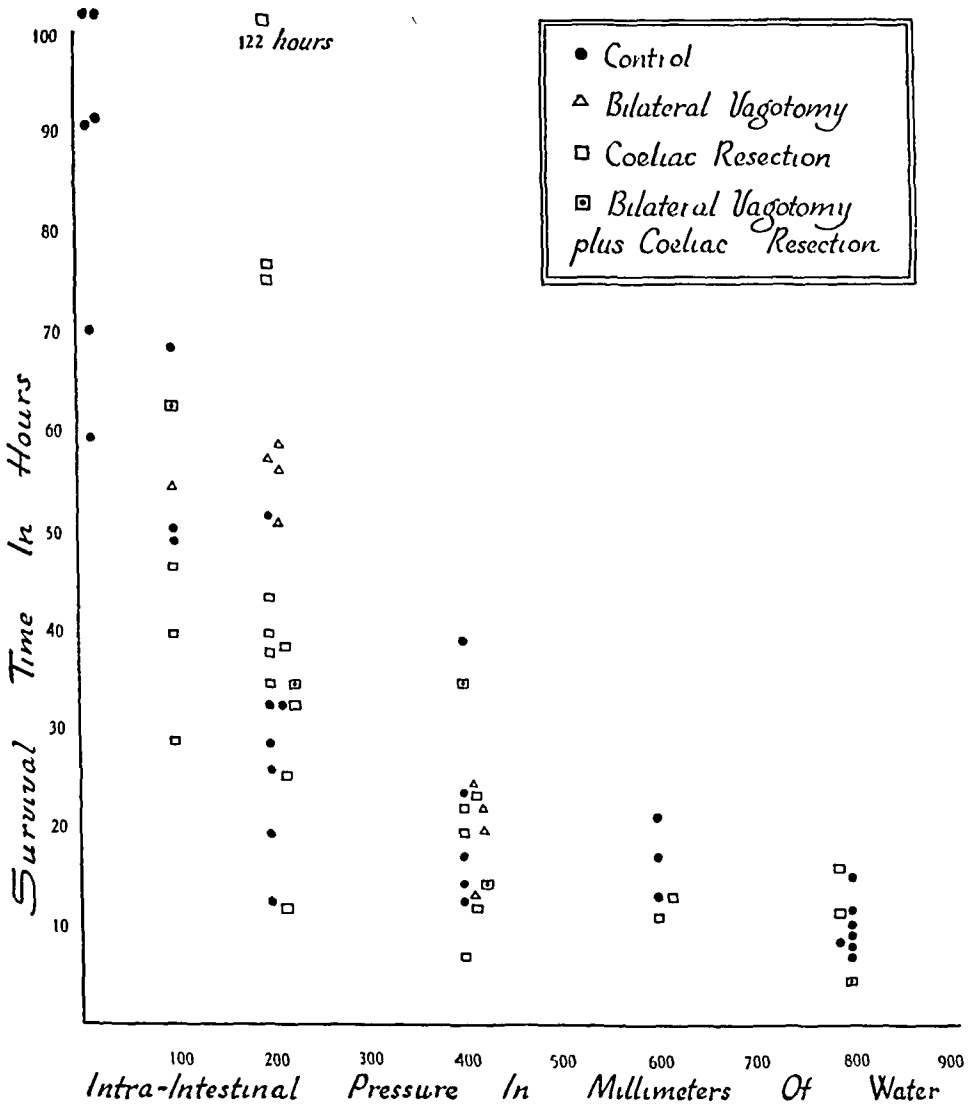


CHART 1 —A comparison of the survival times of cats, with and without deneivation of the gastro intestinal tract, in which the entire small intestine, ligated at both ends, was continuously inflated at various levels of intraluminal pressure

sure, (2) that complete deneivation of the small intestine by resection of the celiac ganglion, with or without bilateral vagotomy, does not prevent or delay the death of the animal from distention

It is furthermore apparent that parasympathetic deneivation (bilateral sub-diaphragmatic vagotomy) does not prevent death or substantially minimize the lethal effect of distention. The results obtained in dogs whose spinal cords were transected at the fourth to the fifth dorsal segments make it clear that

sympathetic denervation also does not delay the extremely rapid death of dogs from distention (Chart 2)

(B) *Effect of Denervation on Fluid Accumulation in the Intestine and Peritoneal Cavity* In Table I, the total fluid content of the small intestine and of the peritoneal cavity has been tabulated under the various experimental conditions studied. The average fluid content of the small intestine of undistended control animals at the time of death is 46 cc. When the intestine is subjected to continuous distention pressures of 100, 200, 400, 600 or 800 Mm. of water

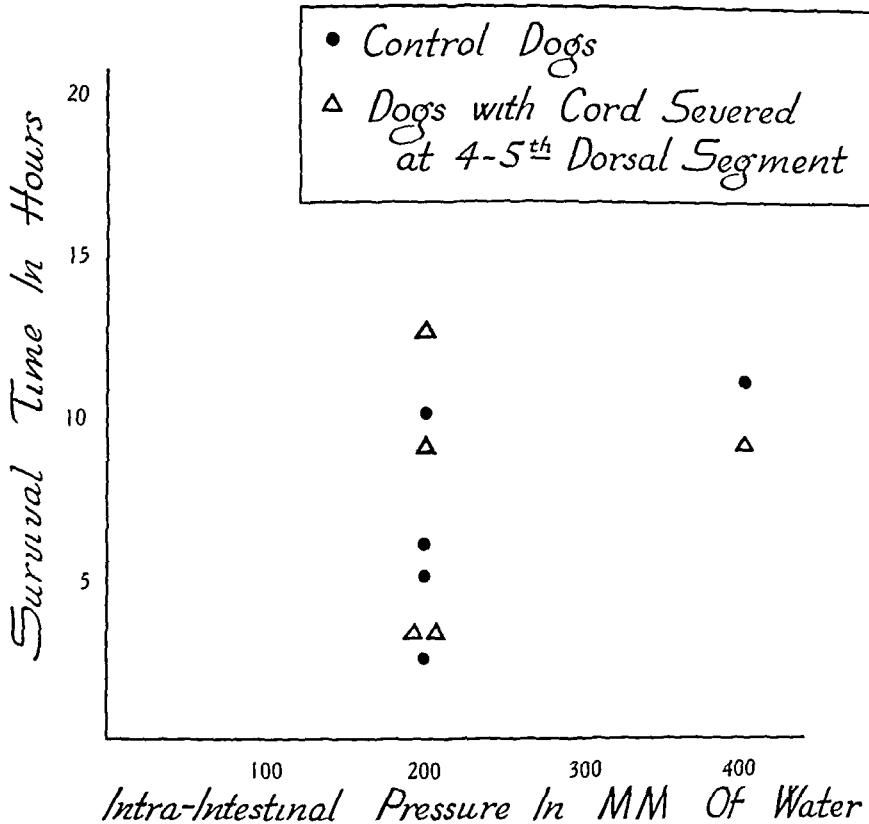


CHART 2—A comparison of the survival times of dogs with and without spinal cord transection in which the entire small intestine ligated at both ends, was continuously inflated at various levels of intraluminal pressure

until death results, the corresponding average fluid volumes are 25, 45, 26, 31 and 11 cc., respectively, in the undenervated animals, and 43, 42, 43, 35 and 14 cc., respectively, in the denervated animals. These figures do not substantiate the prevailing opinion that fluid accumulation in the intestine is caused by an increase of intra-intestinal pressure. Nor do they indicate that the extrinsic nerve supply substantially influences the fluid production in the small intestine of cats dying from acute distention of the entire small bowel.

In a previous paper,⁶ evidence was presented that the loss of plasma into the peritoneal cavity incidental to gaseous distention of the intestine was insufficient *per se*, or in combination with the fluid loss into the bowel wall and lumen, to constitute a primary mechanism in the death from distention. Corresponding data from similar experiments in animals with various types of

bowel denervation show no substantial difference in the results (Table I)

Discussion—In the continuing search for the cause of death from intestinal obstruction a variety of agents have been demonstrated which clearly contribute to the lethal result. But no single pathogenic factor has as yet been demonstrated to be present and operative in *all* types of obstruction and which *per se* can account for the death. The revival of the neurogenic theory, for further elucidation of the cause of death, receives no confirmatory support from the experiments herewith reported. The denervation experiments of Taylor, Weld and Harrison, who used a nonobstructing balloon in the upper jejunum, led them to conclude that their animals were rendered immune to the effects of distention because of a prolongation of the survival time from an average of 29 hours to one of 75 hours, at which time the animals succumbed to peritonitis. The experimental conditions utilized are not comparable to those prevailing in mechanical obstruction and the adverse effects usually associated with obstruction were not observed. Herrin and Meek noted beneficial effects from denervation of Thiry-Vella loops in dogs whose gastro-intestinal tract had been reconstituted. Here, too, the experimental set-up can be related to obstruction only in respect to the presence of a painful stimulus producing anorexia and a loss of water and electrolytes. The extreme degree of distention pressure (650–1300 Mm water) used in the experiments of these investigators^{1, 2} was far in excess of that which is observed in man and presumably caused extreme pain in the undenervated dogs. Their death is conceivably attributable to a state of shock produced by the neurogenic mechanism (prolonged sympathetic stimulation) described by Freeman and implied in the experiments of O'Shaughnessy. Shock, to be sure, appears in the prelethal stages of experimental and clinical mechanical obstruction and, to the extent to which the neurogenic factor operates so as to add to other existing burdens, it may not be ignored. In the light of our experiments, however, obliteration of a neurogenic type of shock will not prevent rapid death in obstruction.

Braun and Borriutau⁷ postulated a neurogenic etiology for the death in obstruction, according to which noxious stimuli reached the brain and produced failure of vasomotor and other vital centers. In evidence, they presented observations of a fall in blood pressure in animals with strangulation obstruction. Continuous tracings of the blood pressure curve in a considerable number of our experiments with simple closed loop obstruction showed a sustained blood pressure until very shortly before death.

Shock due to other than neurogenic causes may be a significant and perhaps all important factor in simple obstruction. Experiments now in progress indicate that the loss of plasma volume, a primary feature of shock, may be alone sufficient to cause death, and that this loss of plasma may occur in the absence of dehydration or loss of electrolytes by vomiting, and in the absence of significant fluid losses into the bowel lumen, bowel wall and peritoneal cavity.

Death from distention, in our experiments, occurred in the absence of a notable loss of fluids and electrolytes into the stomach, bowel wall and lumen.

or peritoneal cavity whether or not the gastro-intestinal tract had been deprived of its extrinsic nerve supply. In both groups the stomach was usually found empty and the fluid in the bowel lumen, bowel wall and peritoneal cavity did not exceed the values found in the undistended controls in amounts sufficient to explain the rapid death from distention.

The conflicting data in the literature as to the relative importance of the various lethal factors involved in obstruction arise from the extremely selective conditions of many of the experimental techniques. The use by so many investigators of a high jejunal or duodenal closed loop, by focusing exaggerated attention on one phase of the processes involved, blurs the picture of the balance of forces usually operating in clinical mechanical obstruction, where one is usually dealing not only with secretory loops, but with absorptive loops in continuity with them. Absorption in the jejuno-ileum, if hindered by increased intraluminal tension, is not, therefore, to be dismissed as not operating at all to counterbalance the activity of the higher secretory loops. Consequently we consider the data from our experiments, utilizing the whole small intestine, as a closer approximation to the facts than the data from the use of small segments possessing a restricted function.

CONCLUSIONS

The survival time of cats with obstruction and gaseous distention of the small intestine is inversely proportional to the level of the pressure in the lumen of the bowel. Preliminary exclusion of the extrinsic nerve supply of the gastro-intestinal tract does not influence the survival time of such animals.

Fluid accumulation in the intestinal lumen, bowel wall and peritoneal cavity in these animals is not sufficient to account for their rapid death. Extrinsic denervation of the gastro-intestinal tract does not significantly alter the fluid volume in the intestine or peritoneal cavity.

REFERENCES

- ¹ Herrin, R. C., and Meek, W. J. Distention as a Factor in Intestinal Obstruction. *Arch Int Med*, **51**, 152, 1933.
- ² Taylor, N. B., Weld, C. B., and Harrison, G. K. Experimental Intestinal Obstruction. *Jour Canad Med Assn*, **29**, 227, 1933.
- ³ O'Shaughnessy, L., and Slome, D. Etiology of Traumatic Shock. *Brit Jour Surg*, **22**, 589, 1935.
- ⁴ Freeman, Norman E. Decrease in Blood Volume after Prolonged Hyperactivity of the Sympathetic Nervous System. *Am Jour Physiol*, **103**, 185, 1933.
- ⁵ Moon, V. H., and Morgan, D. R. Shock, Mechanism of Death Following Intestinal Obstruction. *Arch Surg*, **32**, 776, 1936.
- ⁶ Rosenfeld, L., and Fine, J. The Effect of Breathing 95 Per Cent Oxygen Upon the Intraluminal Pressure Occasioned by Gaseous Distention of the Obstructed Small Intestine. *ANNALS OF SURGERY*, **108**, 1012, 1938.
- ⁷ Braun, W., and Borrutau, H. Experimental kritische Untersuchungen über den Ileustod. *Deutsch Ztschr f Chir*, **96**, 544, 1908.

THE TREATMENT OF VOLKMANN'S ISCHEMIC CONTRACTURE¹

HENRY W MEYERDING, M D

SECTION ON ORTHOPEDIC SURGERY

AND

FRANK H KRUSEN, M D

SECTION ON PHYSICAL THERAPY, THE MAYO CLINIC

ROCHESTER, MINN

THE flexion deformity of the wrist and fingers resulting from contraction and fibrosis of the flexor muscles of the forearm is known as Volkmann's ischemic contracture. Affecting children and occurring as a complication of fractures of the lower end of the humerus, it results in permanent partial or total disability when once it becomes established, despite the most expert surgical and physical treatment.

It is of interest to note that in the articles and reports of cases published since the original report of Volkmann in 1869, no author has claimed a certain method of cure. While there has been some difference of opinion in the past as to the factors involved in the production of the contracture, we believe that the etiology is now better understood and that means of prevention are available.

It is only through the use of conservative stretching and surgical methods that benefit can be obtained in the treatment of long-standing Volkmann's contracture. Without physical therapy, little can be accomplished. In every case of ischemic contracture, whether operation is performed or not, physical therapy is the greatest aid in recovery of a useful extremity. In considering the use of physical measures in the treatment of Volkmann's ischemic contracture, one is impressed with the paucity of information on this particular phase of treatment. In a paper published in 1930, one of us (Meyerding⁷) pointed out that the value of physical therapy cannot be overemphasized and that it should be continued for a considerable period of time.

At The Mayo Clinic a series of 182 cases of Volkmann's ischemic contracture has been observed.⁹ In cases of fracture of the lower end of the humerus the factors leading to the production of Volkmann's ischemic contracture are as follows. The force which breaks off the lower fragment carries the condyles backward and strips the periosteum away from the posterior surface of the proximal fragment, this space promptly filling with blood. The lower end of the proximal fragment is carried forward and downward, piercing the periosteum and forcing its way against the soft tissues, blood vessels and nerves become compressed and hemorrhage infiltrates the antecubital spaces and, if severe, as from a ruptured artery, forces its way into the forearm. Nerves may be severed and paralysis may be noted before

* Read before the meeting of the Western Section, American Congress of Physical Therapy, Los Angeles, Calif., June 9, 1938. Submitted for publication September 9, 1938.

there has been time for an ischemia to develop. Undue roughness or lack of skill in handling may aggravate the injury and increase pressure already present. Muscle-pull holds the overlapping bones in malposition, thus further impairs circulation in the forearm.

The extent of injury up to this time depends on the type of fracture and local injury to soft tissues. Figure 1a shows Volkmann's ischemic contracture of the left forearm of a boy, age 19. The contracture had been present for ten years and had followed an injury to the elbow. At the time of the injury a tight bandage had been applied, this had been left in place for one week. The patient had had severe pain following the application of this bandage. No treatment was given at the clinic. Figure 1b shows Volkmann's ischemic contracture of the left forearm of a boy, age 8. The contracture, which had followed a supracondylar fracture, had occurred six months before the patient was brought to the clinic. At the time of the fracture the arm had been placed in a position of acute flexion, and adhesive tape and bandages had been applied. The patient had complained of severe pain following this treatment but the splint had been left on the arm for five weeks. An operation had been performed to free adhesions about the elbow. Treatment at the clinic consisted of the application of a Jones splint and the use of physical therapy. This treatment produced improvement. Figure 1c shows Volkmann's ischemic contracture of the left forearm of a man, age 20. The contracture had occurred after a supracondylar fracture, eight years before the patient came to the clinic. At the clinic treatment consisted of lengthening of the tendons, manipulation and arthrodesis of the wrist, and the subsequent use of physical therapy. The result was excellent, the patient was able to work and he could hold objects in his hand and use it. If the fracture is not reduced, the result may be malunion with a rather good functional result in the forearm and some limitation of motion in the elbow. Should arterial hemorrhage be unchecked, venous flow is interfered with by the development of a subfascial hematoma, distention, tenderness and induration of the antecubital space, and pain, cyanosis, and loss of pulse and numbness take place. The arm becomes cold and blue, the pulse is absent, blebs appear on the skin, intense pain occurs, and, unless intrinsic pressure is relieved contracture will take place. In a matter of a few hours, not days or weeks, the injury to the muscle fibers has occurred. In the presence of induration in the antecubital space, the first effort should be devoted to relieving the intrinsic pressure rather than reducing the fracture. Excellent results are usually obtained in uncomplicated supracondylar fractures which have been treated immediately by accurate reduction and retention in a position of flexion. Repeated observations of the color of the hand and of the volume of the pulse should be made lest an unrecognized hemorrhage appear and impair circulation. The position of the fragments should be checked to be sure displacement has not occurred.

Malunion occurs in 40 per cent of cases in which a fracture is associated with ischemic contracture. In many instances the displacement occurs dur-

ing attempts to relieve pain and swelling by releasing the retentive dressing. Holding the fracture in acute flexion cuts off circulation and it should be insisted upon that the patient assume the recumbent position, the forearm should be suspended for a few days until reduction can be accomplished more safely. An airplane splint is excellent for ambulatory patients. Patients should not be permitted to be up and about with arms swollen and cyanotic and hanging at their sides. If the patient is seen at a time when the antecubital space is distended and tender and the pulse is faint and the skin is bluish-red in color and there is great pain, all dressings should be removed and the arm should be elevated on pillows with the elbow extended beyond a right angle. Warm, but not hot, moist dressings should then be applied. If within the next hour the swelling increases and the pulse is absent, the condition should be considered serious and preparation should be made for sur-



FIG 1—Volkmann's ischemic contracture, (a) of left forearm of male patient, age 19, (b) of left forearm of a boy, age 8, (c) of left forearm of a man, age 20

gical intervention. In such cases the stage is set for the production of an ischemic contracture. Occasionally, such cases are seen after several manipulations have been performed and considerable time has intervened since the fracture. The arm is then distended to such an extent as to demand immediate relief through surgical measures.

Skeletal traction, by means of a Kirschner wire through the olecranon, is an excellent method of correcting malposition of the fragments and should not, in certain cases, be overlooked as a useful aid, either as a preliminary to exploration of the hematoma or after careful operative inspection of the brachial artery and median nerve. Free incision over the hematoma and through the deep fascia liberates muscle tissue and blood which have been under tension. An incision mesial to the biceps permits the bicipital fascia to be divided close to the tendon, and the artery, vein and nerve can readily be inspected. Complete rupture of the brachial artery has been observed as well as partial or complete severance of the nerve. The deep fascia over the forearm may require division, and this may be done subcutaneously by means

of a special knife. The fracture may be reduced and internal fixation used by means of bone screws or Kirschner wire. The entire arm is then enclosed in a large, moist alcohol and boric acid dressing and is suspended in abduction. If the preventive measures described have been followed, one is in a position to meet the complications following supracondylar fractures and to prevent many of the disastrous complications of ischemic contracture.

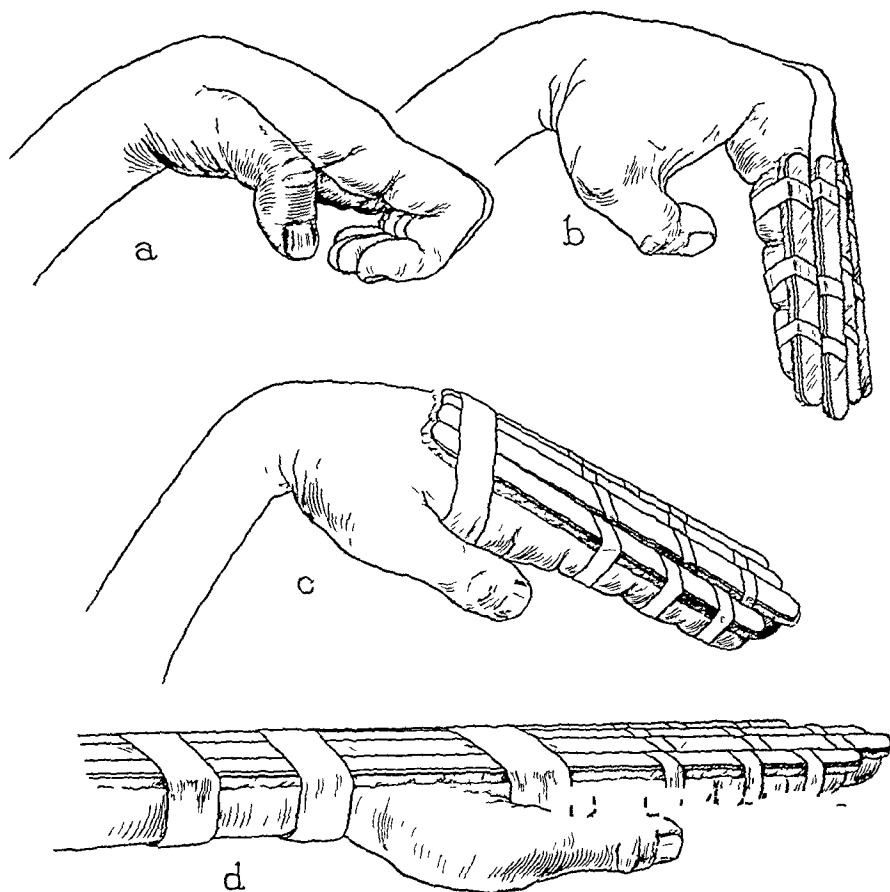


FIG. 2—Economical method of splintage by means of ordinary wooden tongue depressors (a) typical Volkmann's contracture, (b) tongue depressors used as splints to extend the fingers, (c) tongue depressors used as splints to extend metacarpophalangeal joints as well as the fingers, (d) long wooden splints used to extend the wrist and hand. The splints are padded with a thin layer of felt and are loosely retained in position by circular bands of adhesive tape.

CONSERVATIVE TREATMENT OF VOLKMANN'S ISCHEMIC CONTRACTURE—Volkmann's ischemic contracture may occur in a few hours, and the earlier treatment is begun, the better will be the results. After relief of intrinsic pressure, no time should be lost in attempting gradual extension of the involved muscles. During the early stages, in the presence of edema and clots, heat and massage aid the absorption. After the deformity has been present for days or weeks, heat, massage, and gradual extension by splints are preferable, as by this time clots and swelling are subsiding.

Splints are first used to extend the fingers, and later they are employed continuously to extend the fingers and wrist when physical therapy is not being administered.⁸ There has been considerable progress in conservative

treatment² since the general acceptance of the method of Sir Robert Jones, which consists in the gradual, continued stretching of the contracted tissues. This method should be undertaken during the acute stage, which lasts for about a week. If the patient is not seen for weeks or months after the onset of the contracture, plastic operative measures on the soft structures or plastic procedures on the bones must be considered. In cases in which the contracture is severe, operation may be the only means of correcting the deformity and postoperative physical therapy then allows further improvement. In all cases individual conservative treatment (that is, physical therapy) is applied at the same time, either without operative intervention if the patient is seen during the first week, or possibly following operative treatment if he is seen later. With Sir Robert Jones' method the wrist is passively flexed to allow the fingers to extend and each finger is strapped in the extended position by means of a small gutter-splint or by means of an ordinary tongue depressor. The patient thereafter immediately attempts systematic extension of the metacarpophalangeal joints which are contracted (Fig. 2).

In a few days the joints usually stretch sufficiently to allow the application of longer splints, which extend to the wrist. The wrist is still allowed to remain flexed and either a flat metal splint or a thin boxwood splint is used to flatten both the hand and finger. The wrist is then extended a little farther each day and held fixed in the corrected position. Once the finger and metacarpophalangeal joints are straightened, one may use a molded palmar and forearm splint with a hinge at the wrist to assist in the dorsiflexion of the wrist. Occasionally splints which have extension arms and which are fitted with elastic bands that will produce elastic traction may be employed to advantage. In some instances a banjo splint used with rubber bands fastened to adhesive tape on the fingers permits the fingers to be exercised at all times and is most efficient. Such a splint is inexpensive and can be made in a few minutes (Fig. 3). It has been pointed out by Jones and Lovett⁴ that as the contracture yields to this mechanical treatment the hand improves greatly in function, the circulation improves, and the fingers often show a return of voluntary power. However, if the ischemia has caused complete obliteration of the muscle fibers, it is obvious that good function cannot be obtained. Nevertheless, patients are most grateful for relief from the claw deformity which is so conspicuous. The splinting should always be combined with the use of radiant heat, contrast baths, gentle massage, and in some instances with electric stimulation of the muscles. The first few treatments may consist of applications of radiant heat or whirlpool baths combined with light massage. The splints may soon be adjusted and worn during the intervals between treatments, however, motion may be augmented by gentle passive movements and occasionally by electric stimulation. We usually rely, principally, on heat and massage as aids to gradual stretching, and do not believe that painful assistive motion or forceful manipulation under anesthesia is advisable.

Splints—In addition to the methods of splinting which have been mentioned, Milici¹⁰ has described a splint which was constructed especially for

the treatment of Volkmann's contractures. This is a modification of the familiar banjo splint and closely resembles the splint described by Howitt³ for correction of deformities of the hand in the treatment of atrophic arthritis. Howitt's splint in turn is a modification of the splint described by Kahlmeter.⁵ Milici's modification of the banjo splint for treatment of Volkmann's contracture is characterized by the fact that it has a hinge at the wrist joint with a removable pin, which permits separation of the two parts of the splint. At the wrist the two parts of the splint have, on either side, a groove through



FIG. 3—Banjo splint used to maintain extension of the fingers and wrist. Splint is held by adhesive tape attached to the fingers and connected to the splint by rubber bands; this splint may be adjusted to various positions, is economical and permits active movement of the fingers; it can be easily applied by any physician, (a) dorsal view, (b) palmar view.

which a small metal rod can be inserted in such a manner that the distal part of the splint can be immobilized to any desired degree of dorsiflexion by simply bending the rod. Milici recommended that traction be made on the fingers by attaching them to the ring of the banjo splint by means of the so-called Japanese finger-traps (small tubes of soft straw which cling to the finger when it is inserted in one end of the tube and traction made on the opposite end). These finger-traps have been made chiefly as trick toys. In our opinion, they are not as satisfactory as adhesive tape, since they slip off the fingers too readily. We prefer straight, padded tongue depressors for extension of the phalanges and thin, padded boxwood splints for extension of the

metacarpophalangeal joints and flattening of the hand. Thereafter, in most instances we use a molded palmar and forearm splint (with a hinge joint at the wrist and with arms for elastic traction), or occasionally use a modified banjo splint.

Heat—In conjunction with splinting, the use of other physical measures has never been sufficiently stressed. It seems wise to remove the splint once each day, in order that the other physical measures may be applied. Heat from a luminous source (such as a U-shaped baker containing six or eight 60 watt tungsten or carbon filament lamps, placed directly over the elbow, forearm, and hand, or a 250 watt gas-filled tungsten lamp in a cup-shaped reflector, placed at a distance of two feet [61 cm] from the elbow, forearm and hand) should be applied for 20 to 30 minutes. Even better, the whole arm may be immersed for a period of half an hour in a whirlpool bath, which is a bath of whirling, aerated water kept constantly at a temperature of 110° F.

The latter method of applying heat seems most efficacious, as the mechanical effect of the whirling, aerated water apparently aids in the production of a peripheral hyperemia and seems to produce a relaxing action on the musculature by its gentle massaging effect. However, any one of the methods of applying heat, which have been mentioned, may be employed as a preliminary to the massage and manipulation which should be used before reapplication of the splint. If regions of anesthesia are present, heat should be applied with due caution to prevent burns.

Massage—Massage, properly applied, starting with light effleurage (stroking) and progressing to deeper petrissage (kneading) and to friction (a circular, rolling motion to loosen scar tissue and adhesions), may be applied by skilled hands. In the treatment of Volkmann's ischemic contracture, the time to be consumed by such massage will usually be about ten minutes. Mennell⁶ states "Massage treatment is constantly recommended as a remedy for ischemic contracture. It is a slow and tedious affair and cannot be compared in efficacy or rapidity with treatment by splintage. But there is little doubt that massage can hasten the recovery when splintage is used. It should be applied whenever the splint is altered or readjusted in any way." Great care should be taken not to allow the structures that have been kept in a state of tension by the splint to contract appreciably during the treatment. At the same time, it is wise to see that flexion is fully maintained whenever treatments are administered.

Manipulation—Manipulation may be carried out for the most part manually. Occasionally, as mentioned by Jones and Lovett, electric stimulation may be employed. Clinicians have, as a rule, been slow to apply the principles of mechanoelectric stimulation of muscles which were laid down by physiologists years ago. There are available, in most well equipped hospital physical therapy departments, devices which will generate a smooth, not unpleasant, sinusoidal current that will produce rhythmic contractions of muscles in such a way that atrophy is combated to a slight degree, and deep massage and improved circulation are produced. When voluntary muscular action is present,

such stimulation is not necessary, but when a patient cannot, or will not, move the involved muscles, such electric stimulation may prove of some value. If a sinusoidal apparatus is not available, a simple, small faradic coil can be utilized which may prove to be a fair substitute in the few cases of Volkmann's ischemic contracture in which electric stimulation may be required. If electric stimulation is deemed advisable, the time consumed will usually be about five minutes, and sufficient current should be used to produce rather strong rhythmic contractions of the muscles. Such electric stimulation of atrophied muscles should always be given within the limits of fatigue. Fatigue is indicated by slowing of the muscle's response to the electric stimulus. At the first sign of such slowing of muscular contraction, treatment of that particular muscle, or group of muscles, should be stopped at once.

Finally, manual manipulation of the affected arm and hand should be performed. This should consist of passive movements and active assistive exercises. Coulter and Molander¹ have said: "The chief aim of passive movement is to maintain suppleness and by so doing to prevent contractures and the formation of definite adhesions or the general matting of soft tissue. In this manner passive exercise of muscles prepares them for active movement. Stretching of contractures and old adhesions in chronic conditions should not be confused with passive movement. The object of stretching is to loosen contracted ligaments, muscles and adhesions in stiff joints. The technic of such a procedure should be a slow, steady and gradually increasing pull by the operator or with gradually increasing weights. Joint soreness may be produced by such a manipulation, and a short application of heat with light massage will help materially in making the patient comfortable. As a rule, any pain that passes off in an hour is not detrimental to the final success of the treatment. If there is an increase of swelling and pain or the range of motion is less the next day, too much has been attempted. The angle of movement should always be recorded by using a goniometer, and never estimated by the eye of the operator."

While continuing careful stretching of the contracted muscles, the operator should progress as rapidly as possible to the stage of active assistive exercise (exercise in which the patient makes the voluntary effort to move the affected part and is aided in further motion by the operator). As the patient's condition improves, active motions will become more and more established, and the assistive phase will diminish. Specifically, in the treatment of Volkmann's ischemic contracture the operator should attempt each day, during the time that the splint is off, to carry as nearly as possible each involved joint through its normal range of motion, bearing in mind the precautions just mentioned. The elbow, wrist, and finger joints should each be carried slowly through one single arc of motion. A single slow movement through the entire possible range of movement of the joint is much to be preferred to a series of short, jerky movements through a smaller range.

It should be remembered that Jones and Lovett stressed the importance of maintaining supination of the wrist, and the operator should direct espe-

cial attention to supination and pronation of the wrist as well as to extension and flexion

The time to be consumed by manual manipulations in this particular disease will be approximately five minutes

Finally, if and when function has been sufficiently restored, active exercise in the form of occupational therapy may be instituted. In Volkmann's ischemic contracture, three forms of occupational therapy are particularly indicated: (1) For the fingers, use of the hand loom, weaving, or basketry, (2) for the wrist, block printing, and (3) for the elbow, the use of a large floor loom, the affected arm being flexed and extended while at work with the beater of the loom.

SUMMARY

Volkmann's ischemic contracture is usually associated with supracondylar fractures which have been treated by placing the arm in acute flexion. In the presence of swelling and hemorrhage, acute flexion tends to impair circulation by increasing pressure in the antecubital space, even though the fracture has been reduced. Reduction of the fracture may be deferred for several days, the treatment being directed to the care of the injury to the soft parts in order to preserve function. Elevation of the arm hastens the relief of swelling when the patient is in the recumbent position, and abduction on an airplane splint is most beneficial when the patient is ambulatory. Incision and drainage of large hematomata may be indicated. Reduction and internal fixation of the fracture following removal of blood clots are advisable and are useful measures in preventing impaired circulation. Prevention of an ischemic contracture is possible in many instances provided the patient is seen in time and the utmost care is used to combat injury from circulatory stasis. Conservative methods of treatment such as the stretching method advised by Sir Robert Jones, that is, constant stretching with proper splints in conjunction with heat, massage and proper manipulation, produce the best results in cases in which the condition is recognized before extensive injury to soft tissue and malunion have occurred.

Severe deformities of long standing also require surgical intervention which is then followed by physical treatment. Intrinsic or extrinsic pressure from various causes cuts off the venous blood flow but permits some arterial flow. The formation of blood clots results in sufficient pressure to cause an ischemic paralysis. Placing the arm in acute flexion, malposition of fragments, or pressure (of bandages, splints or casts) may be a contributory factor in impairing the circulation and producing a hematoma and a subsequent Volkmann's contracture. We recognize the great value of physical therapy in the treatment of Volkmann's ischemic contracture and employ it with satisfactory results in practically all of our cases, whether surgical treatment has been carried out or not.

REFERENCES

- ¹ Coulter, J. S., and Molander, C. O. *Therapeutic Exercise. Handbook of Physical Therapy.* Chicago, American Medical Association, 89-102, 1930.

- ² Goldberg, Harry Volkmann's Contracture, Its Causes and Treatment Kentucky Med Jour, 31, 531-537, November, 1933
- ³ Howitt, Frank Correction Appliance for Fingers and Wrist Lancet, 2, 1394-1395, December 22, 1934
- ⁴ Jones, Robert, and Lovett, R W Orthopedic Surgery Ed 2, New York, William Wood and Co, pp 807, 1929
- ⁵ Kahlmeter, Gunnar An Apparatus for the Treatment of Deviations in the Metacarpophalangeal and Interphalangeal Articulations Acta rheumatol, 5, 5, September, 1933
- ⁶ Mennell, J B Massage, Its Principles and Practice Ed 2, Philadelphia, P Blakiston's Son and Co, pp 535, 1920
- ⁷ Meyerding, H W Volkmann's Ischemic Contracture J A M A, 94, 394-400, February 8, 1930
- ⁸ Meyerding, H W Volkmann's Ischemic Contracture Physiotherapy Rev, 12, 96-97, March-April, 1932
- ⁹ Meyerding, H W Volkmann's Ischemic Contracture, Associated with Supracondylar Fracture of Humerus J A M A, 106, 1139-1144, April 4, 1936
- ¹⁰ Milici, Attilio Treatment of Volkmann's Ischaemic Paralysis by Elastic Traction Report of Seven Cases Jour Bone and Joint Surg, 31, 516-526, April, 1933

SOLITARY MYELOMA OF BONE*

A CLINICAL AND PATHOLOGIC ENTITY

JOSEPH G PASTERNAK, M D

CHIEF OF PATHOLOGIC SERVICE

AND

RICHEY L WAUGH, M D

CHIEF OF SURGICAL SERVICE,
UNITED STATES MARINE HOSPITAL

NEW ORLEANS, LA

FROM THE UNITED STATES PUBLIC HEALTH SERVICE, UNITED STATES MARINE HOSPITAL, NEW ORLEANS, LA

MULTIPLE myeloma with its hopeless prognosis is a familiar disease. Solitary myeloma of bone, however, with its more favorable prognosis, is not so well known or so readily recognized. Observations on this disease have multiplied during the past few years and it seems to be fairly well, if not finally, established that it is a distinct and important clinical and pathologic entity, to which a relatively recent editorial¹ called attention.

A critical review of the literature disclosed that some of the recorded cases of a single myeloma of bone are not well authenticated. To substantiate a diagnosis of solitary medullary myeloma, the following proofs are indispensable: (1) Histologic examination of the tumor by a competent pathologist; (2) Either careful roentgenologic examination of the entire skeleton or complete and thorough necropsy. It is realized that occasionally bones may contain histologically demonstrable foci of myeloma which were not evident in the roentgenogram. However, sooner or later such foci do become roentgenologically demonstrable.

On the basis of these criteria, 30 cases of solitary myeloma, with and without subsequent generalization of the disease, have been collected from the literature. An analysis of these cases and a new case, that has been under observation for seven and one-half years, are presented.

Case Report—J F, male, white, age 46, seaman, was admitted to U S Marine Hospital, New Orleans, October 10, 1936, complaining of swelling, stiffness, and pain in the left shoulder. In November, 1929, the patient fell and sustained an injury to the left shoulder. On January 10, 1930, while fighting, his arm "just dropped" and his left shoulder became very painful. He entered a hospital January 11, 1930, where a diagnosis of a pathologic fracture of the left humeral neck was made, which was verified roentgenologically. Manipulation was undertaken and a Thomas splint applied. Roentgenograms on January 23 and 30 showed displacement of the fragments and callus formation. Reexamination of the films on February 4, 1930, resulted in the opinion that this was a "pathologic fracture occurring in an area with destruction, probably due to endothelioma." High voltage radiation was prescribed. Roentgenograms, February 14, 1930, showed no evidence of malignant metastases to other bones of the skeleton.

* Approved by the Bureau of the United States Public Health Service, June 10, 1938.
Submitted for publication August 20, 1938.

Subsequent roentgenologic examinations showed March 3, 1930 "Considerable new callus formation with practically complete union of the fragments. The head of the humerus is a little more dense than on the previous examination. There is considerable spotty decalcification of the upper two-thirds of the humeral shaft. This is probably due to extension of the tumor." More radiation therapy was prescribed.

March 31, 1930 "Considerable new callus formation since previous examination. Bony union is practically complete. There has been no extension of the process."

April 10, 1930 "There is further regeneration of bone."

In all, five deep roentgen ray treatments were administered. The patient resumed his duties as a seaman and worked until December, 1934, when he fell and again injured his left shoulder. He was admitted to a hospital December 26, 1934. He was told that he had a bone cyst and was given out-patient treatment until April 4, 1935. He continued to work but with increasing difficulty. In August, 1936, he entered a hospital

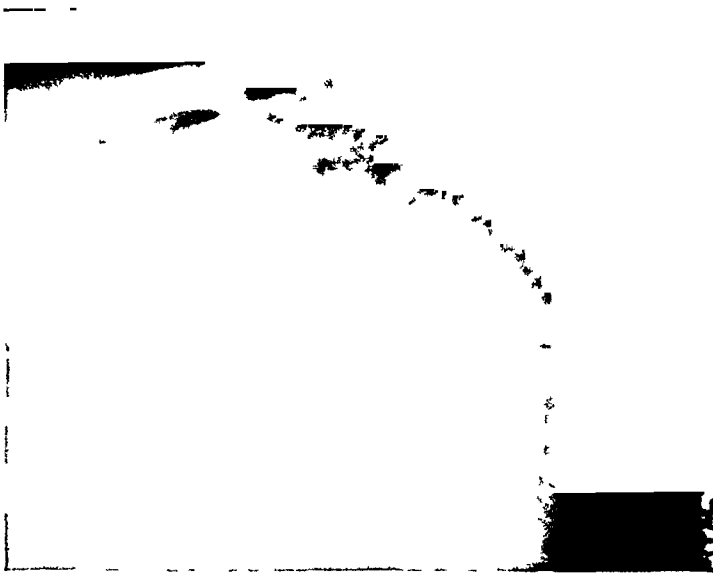


FIG 1.—Roentgenogram of the left humerus showing bone destruction, trabeculation and cortical expansion. Roentgenologic Diagnosis: Giant cell tumor. Histologic Diagnosis: Plasma cell myeloma.

because of considerable swelling of the shoulder, and was transferred to the U. S. Marine Hospital, New Orleans, October 10, 1938, for further study and treatment.

Physical Examination—The patient appeared well, although he had lost about 20 pounds of weight. There was a rounded enlargement of the upper end of the left humerus. The swelling was regular and fairly symmetrical. It was firm and only slightly tender. The muscles of the left arm and shoulder girdle showed marked atrophy. Shoulder movements were markedly limited, apparently due to complete fixation of the scapulohumeral joint. *Roentgenologic Diagnosis*: Giant cell tumor of head of humerus (Fig. 1). Repeated examinations of the urine showed no Bence-Jones protein or other abnormalities. Examination of the blood showed no abnormal hematologic findings. Wassermann and Kahn tests were negative.

Operation—Upper end of humerus was resected November 4, 1936.

Pathologic Examination—*Gross*: The specimen consists of the proximal end of the humerus at the surgical neck. It is expanded into a pyriform swelling measuring 8 cm. in its greatest diameter. It is elastic and crackles and crunches on pressure. The periosteum bulges. In some areas it is thin and in others it is considerably overgrown by old fibrous tissue. The articular cartilage is torn and elevated at the margin.

The opened specimen shows the cancellous tissue of the head and neck entirely

replaced by dark red, friable, soft and firm, hemorrhagic, infarcted tissue that crumbles between the forceps. Here and there the clot contains pieces of gritty material.

The cortical bone is of eggshell thinness and shows numerous fractures and interruptions, the periosteum forming the only retainer. The periosteum is apparently infiltrated by tumor and discolored by blood pigment but the growth does not extend through it.

Microscopic—Frozen sections were stained with 0.3 per cent toluidine blue. O. Paraffin sections were stained with Weigert's acid iron chloride hematoxylin and Van Gieson's picrofuchsin, a buffered Romanowsky stain²⁵ and a modification of Foot's stain for reticulum.

The parenchyma of the tumor is compact, diffuse in character and of uniform cell structure. It is formed of typical plasma cells. They average 11μ in diameter. In areas, degenerating cells showing pycnosis and fragmentation of the nucleus are seen. Plasma cells containing two and three nuclei occur here and there. Cells exhibiting

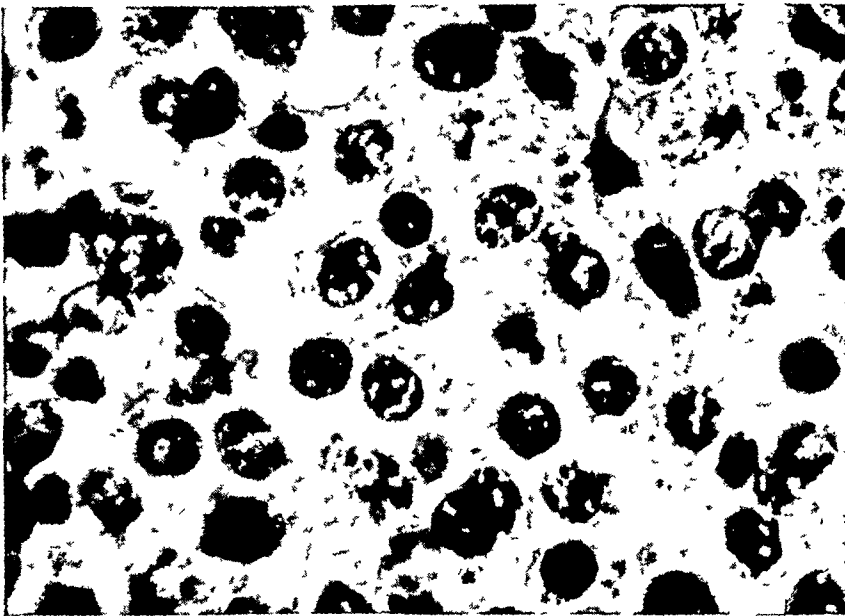


FIG. 2.—Photomicrograph showing plasma cell myeloma of the humerus (High power.)

mitotic figures are occasionally seen. Small lymphocytes and cells with lymphoblastic nuclei are encountered in some areas. In a few areas a delicate fibrillar stroma is discernible but an argyrophilic reticulum could not be demonstrated (Fig. 2).

The solid masses of cells are interrupted by ramifying sinusoids and cystic spaces of various sizes filled with blood. The latter are often separated from each other and lined by one or more orderly rows of plasma cells. Numbers of plasma cells also occur mixed with the blood. Old and recent disorganizing hemorrhages are present. In parts of the tumor the parenchyma is roughly lobulated by strands of fibrous tissue from the periosteum. These strands often carry large, well-formed blood vessels.

Along the periosteum and occasionally within the tumor thin, deformed and rarefied fragments of dissolving bone are present. Rarely a spicule is lined by several osteoclasts or a chain of osteoblasts. Stretches of the periosteum are split into fine strands by infiltrations of solid masses of plasma cells. Occasionally the periosteum shows foci of active proliferation. In areas, it is overgrown by vascular and fibrosing granulation tissue infiltrated by lymphocytes and contains deposits of old blood pigment. Stretches of the periosteum are thickened and converted into old, hyalinized scar tissue.

Follow-Up—Roentgenologic examination of the entire skeleton November 18, 1936, and March 2, 1938, showed no secondary foci. Repeated uranalyses have remained

TABLE I
RESUME OF REPORTED CASES OF SOLITARY MYELOMA OF BONE

Age Sex	Primary Site	Radiographic Appearance	Protein Bence-Jones	Period From Onset	Period Ob- served	Pain	Swelling	Patho- logic Fracture	Treatment	Prognosis
Adult M ² 41 F ³	Clavicle, right, outer third Maxilla	Giant cell tumor or cyst Defect in alve- olar process	+	13 mos	Several mos	+	+	o	Resection	2 mos later secondary focus in 1 rib Outcome not given
29 M ⁴	Humerus, right, middle third	Giant cell tumor	o	1 wk	9 yrs	+	?	+	Curettage	No recurrence or generaliza- tion after 9 yrs
55 M ⁵	Vertebrae, 7th cervical, 1st thoracic		?	7 mos	1 mo	+	?	?	Laminectomy	Died postoperatively
68 F ⁶	Femur, left, upper third	Giant cell tumor or cyst	?	12 mos	Days	+	?	+	None	Died of heart disease
56 F ⁷	Femoral neck, left	Giant cell tumor or cyst	o	4 mos	2 yrs	+	+	o	Disarticulation	No recurrence or generaliza- tion after 2 yrs
33 M ⁸	Vertebra, 4th thoracic	None	?	6 wks	?	+	?	o	Laminectomy	Died of hemorrhagic cystitis, infarcts and abscesses of right lung
34 M ⁹	Femur, right	Giant cell tumor	o	7 mos	4½ yrs	?	+	+	Curettage, ra- dium puncture and amputation	No recurrence or generaliza- tion after 4 yrs
45 F ¹⁰	Femur, left, upper third	Bone destruc- tion	o	2 mos	?	+	?	Postop- erative	Biopsy and crui- terization	Outcome not given
51 M ¹¹	Iliac bone (pos- terior part)	Giant cell tumor	o	11 mos	3 yrs	+	+	o	Excision	Massive infiltrating tumor Local recurrence after 3 yrs
49 F ¹¹	Iliac bone	Giant cell tumor	o	3 yrs	Few mos	+	+	-	Biopsy	Tumor inoperable shortly after coming under observation

SOLITARY MYELOMA OF BONE

Case No.	Age	Sex	Site of Lesion	History	Duration	Findings	Treatment	Outcome
58	M 12	F	Femur, upper third	Giant cell tumor	2 yrs	+	Radium pack, Coley's toxins	Generalization and death after 2 yrs
60	M 13	F	Femur, left, at level of lesser trochanter	Giant cell tumor	6 mos	+	Disarticulation	Died of surgical shock
34	M 14	F	Humerus, right, upper third	Giant cell tumor	8 yrs	+	Amputation	No recurrence or generalization after 8 yrs
43	M 14	F	Maxilla	Giant cell tumor	5 mos	+	Excision	Tumor of forehead 3 mos later
62	F 15	F	Femur, left, upper third	Cystic tumor	6 mos	+	Excision	Disappeared after short course of X-ray
36	F 16	F	Ilium	Cystic tumor	6 mos	+	Curettage	No recurrence or generalization after 8 yrs
49	M 17	F	Vertebra, 6th thoracic	Compression and rarefaction	12 mos	+	None	Became cachectic and died 2 mos later
38	F 17	F	Parietal bone, left	Cranial defect	4 mos	+	Laminectomy, radium and X-ray	Died of cerebral hemorrhage
65	M 18	F	Parietal bone, right	Giant cell tumor or cyst	18 mos	+	Excision	Multiple myeloma 19 mos later
49	F 19	F	Ilium, right	Giant cell tumor	8 mos	+	Excision	Multiple myeloma 2 mos later (6 mos after the appearance of the primary tumor)
19 mos	F 20	F	Femur, left, upper third	Giant cell tumor	6 wks	+	X-ray	No recurrence or generalization after 18 mos
					20 mos	+	Exploration and X-ray	Outcome not given
						?		Secondary focus in skull 7 mos later
								After X-ray therapy, primary lesion and secondary focus disappeared
								No recurrence or generalization after 20 mos

TABLE I (Continued)

Age Sex	Primary Site	Radiographic Appearance	Protein Bence-Jones	Period From Onset	Period Ob- served	Pain	Swell- ing	Patho- logic Fracture	Treatment	Prognosis
50 M ²¹	Humerus, right	Giant cell tumor or cyst	o o	6 mos	9 mos	+	o	o	X-ray	Free from pain and doing well after 9 mos
39 M ²²	Tibia, right, junction middle and upper third	Giant cell tumor	o o	3 mos	5 mos	+	+	+	X-ray and amputation	No recurrence or generaliza- tion after 5 mos
39 F ²³	Humerus, left	Giant cell tumor	+	2 yrs	23 mos	+	+	o	X-ray	Died of chronic nephritis and pulmonary abscesses
58 M ²³	Humerus, right	Trabeculation and areas of density	? ?	19 mos	-	-	+	o	X ray	No recurrence or generaliza- tion after 20 mos
52 M ²³	Vertebra, 2nd lumbar	Giant cell tumor	- o	?	10 yrs	+	-	-	X ray, stabili- zation opera- tion	After 10 yrs disease still present in the original ver- tebra and the adjacent ones only
56 M ²³	Femur, right, upper end	Giant cell tumor	o +	1 mo	33 mos	+	-	At time of biopsy	Curettage	Was considered a giant cell tumor In excellent health 2 yrs later Multiple myel- oma and death after 3 yrs
57 M ²³	Humerus, right, upper end	Destructive lesion	o +	7 mos	28 mos	-	-	+	Resection	Multiple myeloma 10 mos later
65 M ²⁴	Humerus, right, upper third	Extensive honey- combing	o o	10 yrs	7 yrs	+	-	+	X-ray	No recurrence or generaliza- tion after 7 yrs
46 M ²⁵	Humerus, left, upper end	Giant cell tumor	o o	2 mos	8 yrs	+	+	+	X ray and re- section	No recurrence or generaliza- tion after 7½ yrs

Key letters

+ Indicates present

o Indicates none present

- Indicates not stated

?

Indicates information indefinite, neither positive nor negative statement made in article

negative for Bence-Jones protein. The patient has gained over 20 pounds in weight since the operation, appears robust and feels strong.

Analysis of Reported Cases—Table I presents, in brief, the important data from the recorded cases.

Trauma—A history of old or recent injury of the part was recorded in approximately one-half of the cases. In a few, injury preceded the disease by an interval sufficiently long to consider it of some significance, but in the majority, the trauma was evidently superimposed upon an already diseased bone, in that roentgenograms made shortly after the injury disclosed bone destruction or pathologic fracture.

Pain—Pain localized to the affected area was an early symptom in 23 (74 per cent) cases. It was more or less constant, progressive in character but recorded as severe in only several of the cases, notably those in which the iliac bone was involved.

Swelling—Slight to moderate swelling was recorded in 15 (48 per cent) cases. Marked deformity was present in several patients.

Pathologic Fracture—Fracture occurred in 13 (42 per cent) cases. It was spontaneous in six cases, followed trauma in five, developed at time of biopsy in one case and shortly after operation in one case. Pain preceded pathologic fracture by weeks or months.

Disability—In the majority of cases disability was out of all proportion to the pain and deformity.

Age—The youngest patient was a female, age 19 months, and the oldest a woman, age 68. Excluding the infant, the average age of the recorded cases is 49 years.

Gilmore²⁶ reported multiple myeloma in a little girl, which he stated began as a lesion of the right orbit at the age of 18 months.

Sex—Twenty of the cases were males and 11 females.

Bones Involved—Femur, nine cases, ilium, seven cases, humerus, five cases, vertebra, four cases, maxilla, two cases, parietal bone, two cases, tibia, one case, and clavicle, one case.

Bence-Jones Proteinuria—This was found in four (13 per cent) of the cases at the time of the solitary lesion. In two cases it appeared after the disease had become generalized.

Roentgenographic Appearance—Solitary myeloma presents two rather characteristic types of roentgenographic appearances. In 19 (66 per cent) of the cases the roentgenogram was that of a giant cell tumor or bone cyst. The majority of the remainder suggested metastatic carcinoma.

Thus we have a new disease entity that often presents the interesting clinical behavior and roentgenographic appearance typical of giant cell tumor. Not all bone lesions giving a roentgenographic appearance typical of giant cell tumor or cyst prove to be that on microscopic examination. In order to make a correct diagnosis, a biopsy and histologic examination are necessary.

Coley²⁷ has stated "The importance of knowing the nature of the tumor before prescribing the type of treatment to be employed far outweighs the so-called disadvantages of a biopsy." However, the biopsy should be the last step in the diagnosis of a bone tumor, after all the other aids to diagnosis have been employed.

Cell Type—The tumor was clearly plasma cell myeloma in 28 (90 per cent) cases. In 26 cases the diagnosis was made from biopsy, and in four from autopsy material. In the tissue from Cabot's⁸ case, Tracy B. Mallory saw areas in which plasma cells were suggested. In two cases^{2, 20} the cells are designated only as myeloma cells.

Treatment and Prognosis—Table I shows that the reported cases were treated by varied methods. For example, cases treated only by curettage,⁴ by amputation¹⁴ or by roentgenotherapy²¹ showed no recurrence or secondary foci after nine, eight and seven years, respectively. Because of the limited number of cases observed, one cannot draw conclusions as to the preferred treatment.

The important fact is that although the treatment used varied widely, five patients showed cure or arrest of the disease and no secondary foci after four, seven, seven and one-half, eight, and nine years. Fifteen patients under observation less than three years showed no secondary lesions. The time interval in these cases was too short to justify a significant conclusion.

One patient originally treated by roentgenotherapy followed by a stabilizing operation was observed over a period of ten years. On the last examination it was found that the disease was still confined to the original vertebra and the adjacent ones.

In two cases, secondary single foci appeared in the skull three and seven months after diagnosis of the primary lesion. Following roentgenotherapy the secondary foci in the skull vanished and no other lesions developed after 20 months and eight years, respectively.

Multiple myeloma developed in six cases at varying time intervals after the diagnosis of the solitary lesion.

Upon analyzing Table I, it is evident that even though a primary single lesion is recognized and presumably adequately treated, a secondary focus may arise or typical multiple myelomata may develop at some later date.

The question naturally arises whether the cases with single lesions that remained solitary over a period of years will not subsequently develop multiple myelomata. In Table I there will be found cases which developed multiple myelomata after varying intervals, the longest, two years nine months following the primary single lesion.

Notwithstanding this, it is reasonable to assume that multiple myelomata will probably not develop in that group of cases that have been under observation for four to ten years and have shown no recurrence or secondary foci. These may be called true solitary myelomata.

SUMMARY AND CONCLUSIONS

An analysis of 30 cases of solitary myeloma of bone, critically selected from the literature, is presented and a new case, that has been under observation for seven and one-half years, is reported.

The cases of solitary myeloma are separable into two groups (1) Those in which the disease began as a solitary lesion but in which subsequently a secondary focus or typical multiple myelomata developed, and (2) those which, after prolonged observation (four to ten years), remained cured or arrested and did not give rise to secondary foci. These may be called true solitary myelomata.

Solitary myelomata often present the interesting clinical behavior and roentgenographic appearance typical of giant cell tumor or bone cyst. Hence, this disease should be considered when roentgenograms of giant cell tumors and bone cysts are studied.

Although true solitary myeloma is a relatively rare disease, it is important to remember that it does occur, that it is amenable to treatment, and that the prognosis is good.

BIBLIOGRAPHY

- ¹ Editorial. The Problem of Myeloma. *J A M A*, 104, 1420, April 20, 1935.
- ² Bloodgood, J. C. Bone Tumors. *Progressive Medicine*, 8, 229, 1906.
- ³ Wallgren, A. Untersuchungen über die Myelomkrankheit. *Upsala Lakaref. förh.*, 25, 113, September, 1920.
- ⁴ Shaw, A. F. B. A Case of Plasma Cell Myeloma. *J. Path. and Bact.*, 26, 125, January, 1923.
- ⁵ Walthard, B. Zircumscriptes myelogenes Plasmocytom der Wirbelsäule. *Schweiz. med. Wchnschr.*, 54, 285, March 20, 1924.
- ⁶ Zdansky, E. Ein Fall von Plasmocytom. *Fortschr. a. d. Geb. d. Röntgenstrahlen*, 36, 368, August, 1927.
- ⁷ Martin, J. F., Dechaume, J., et Levrat, M. Plasmocytome du Col fémoral. *Bull. Assoc. franç. p. l'étude du Cancer*, 17, 539, November, 1928.
- ⁸ Cabot, R. C. (Case 16482) An Unusual Medical, Surgical and Neurological Case. *New England J. Med.*, 203, 1090, November, 1930.
- ⁹ Rogers, Herbert. A Case of Solitary Plasma Cell Myeloma. *Brit. J. Surg.*, 17, 518, January, 1930.
- ¹⁰ Geschickter, C. F. Multiple Myeloma as a Single Lesion. *ANNALS OF SURGERY*, 92, 425, September, 1930.
- ¹¹ Mercier, Catherine. Contribution à l'étude des Sarcomes Plasmocytaires. Thèse Université De Lausanne Institut d'Anatomie Pathologique, 1930.
- ¹² Coley, W. B. Multiple Myeloma. *ANNALS OF SURGERY*, 93, 77, January, 1931.
- ¹³ Harding, W. G., Jr., and Kimball, T. S. Solitary Myeloma (Plasmocytoma) of the Femur. Report of One Case. *Am. J. Cancer*, 16, 1184, September, 1932.
- ¹⁴ Stewart, M. J., and Taylor, A. L. Observation on Solitary Plasmocytoma. *J. Path. and Bact.*, 35, 541, July, 1932.
- ¹⁵ Charbonnier, A., et Mermod, A. Un Cas de Myelome Solitaire du Femur. *Rev. Med. de la Suisse Rom.*, 54, 699, June, 1934.
- ¹⁶ Satanowsky, Sara, Gonzales, J. C. L., and Velazquez, J. G. Luxacion Patologica Intrapelviana del Femur por Plasmocitoma. *La Prensa Medica*, 21, 1900, October 10, 1934.

- ¹⁷ Peyton, W T Effect of Radium on the Spinal Cord, Report of Two Cases of Myeloma Am J Cancer, 20, 558, March, 1934
- ¹⁸ Mathias, Ernst Zur Myeloma Frage Beitr z klin Chir, 161, 79-87, 1935
- ¹⁹ Pohle, E A, and Stovall, W D Plasma Cell Myeloma of the Right Ilium Roentgenologically Mistaken for Giant Cell Tumor Radiology, 25, 628, November, 1935
- ²⁰ Mancini, G Difficolta Diagnostiche in un Raro Caso di Myeloma Solitario dello Scheletro Chir d org di movimento, 20, 370, November, 1935
- ²¹ Liebman, Charles, and Goldman, Sol E Solitary Myeloma of the Ilium Canad M A J, 34, 511, May, 1936
- ²² Chesterman, J T Solitary Plasmocytoma of Long Bones Brit J Surg, 23, 727, April, 1936
- ²³ Cutler, Max, Buschke, Franz, and Cantil, S T The Course of Single Myeloma of Bone Surg, Gynec and Obstet, 62, 918, June, 1936
- ²⁴ Bailey, C O Plasma Cell Myeloma of the Humerus Treated by Roentgen Radiation Am J Roentgenol, 36, 980, December, 1936
- ²⁵ Lillie, R D, and Pasternack, J G Romanowsky Staining with Buffered Solutions II Current Modification J Tech Methods, 15, 65-70 March, 1936
- ²⁶ Gilmore, M E Multiple Myeloma Syndrome in a Child Texas State J Med, 21, 358-362, October, 1925
- ²⁷ Coley, W B Endothelial Myeloma or Ewing's Sarcoma Am J Surg, 27, 7-18, January, 1935

AN OPERATION FOR THE CURE OF FLATFOOT

BEN L. SCHOOLFIELD, M D

DALLAS, TEXAS

THE OPERATION to be described was first performed by the writer in December, 1926. A résumé of his observations was published¹ in 1928. In March, 1936, the operation was performed before a group of surgeons attending a regional meeting of the American College of Surgeons in Dallas. It has the distinction of being a restorative measure as compared with those operations which depend upon arthrodesis (joint destruction) for their success. The loss of resiliency and motion incident to these arthodeses must be quite apparent.

Weak foot (flatfoot) is a condition which, under the influence of weight-bearing, is characterized, anatomically, by a valgus attitude and clinically, by early fatigue. Depression of the longitudinal arch, while often noticed, may be very slight even in cases clinically serious.

Etiology—It is reasonably certain that the majority of cases have a congenital basis, although the symptoms are frequently not apparent until such time as increased weight or activity or debilitating disease calls attention to them. The influence of trauma, rickets and such deformities as bowlegs and knock knees is not to be overlooked. The faulty transference of weight in such deformities is doubtless a factor in the production of symptoms and perhaps of deformity as well. The custom of walking with the toes turned outward is, at least, conducive to the onset of symptoms. Certain individuals of generalized ligamentous relaxation ("loose-jointed") are exceptionally prone to the affection.²

Morbid Anatomy—An accurate knowledge of certain features of the normal anatomy of the bones and ligaments of the tarsus and their interrelation, is essential to a logical understanding of the pathology. Roberts³ called attention to the "rounded under surface of the os calcis, its small bearing area" and the strong ligamentous connection between this bone and other bones of the tarsus. He went into some detail as to the mechanics of weak foot as based on these important considerations. The author has gone a step further. The os calcis (calcaneus) is approximately of the same width as the astragalus (talus) at the level of the subastragalar joint, but below the sustentaculum tali, or overhanging shelf of the heel bone, it becomes narrowed at the expense of its medial side. Hence the weight-bearing part of the heel bone is off-center with reference to the astragalus and tibia. In other words, a vertical line drawn down the middle of the tibia behind, and passing through the center of the astragalus will necessarily fall toward the medial aspect of the bearing surface of the os calcis (Fig. 1). This line represents the course of the center of weight or gravity below the knee, the fibula being for

practical purposes a brace or strut on the side of the leg and ankle. It is seen that a mechanical situation exists which gives rise to a natural tendency of the heel bone to deviate or rotate outward under body weight. The restraining hold of the medial ligament of the ankle joint (deltoid) prevents such deviation in normal feet. Thus it is seen that a too-long or overstretched deltoid ligament is the basis for all weak feet. The scaphoid (navicular) bone reaches a lower level, the os calcis tilts outward below and with these the rest of the bones of the foot follow suit. This is not to say that in traumatic weak foot, certain other factors may not enter the picture, as in poorly treated Pott's fracture, *etc*.

Spasticity of the peronei muscles is a sequence and not a primary cause of the pathology. The same is true of arthritis, infectious or otherwise. A short tendo achillis is a frequent concomitant condition, swelling and congestion are not infrequent.

Symptoms—Early fatigue in the erect attitude is a constant symptom quite often the only subjective one present. This is particularly true in early childhood, when it may be noted that patients will not play long in the erect attitude. In standing, children often flex the great toe sharply so that the medial border of the foot is raised, thus unwittingly correcting the position of the foot. Pain is more often present in adolescents and adults seeking relief and its location is somewhat variable. It may be confined to the medial border of the foot in the vicinity of the deltoid ligament, to the lateral border about the tip of the external malleolus, to the undersurface of the heel and plantar fascia or it may be quite general throughout the foot. More remote pain may be felt in the lower back, hips, medial sides of the knees or the calves of the legs. This is due to the strain incident to malalignment of the feet or to a



FIG. 1—Posterior view of the ankle joint (Cunningham). Vertical line connecting center of tibia above with center of astragalus and continued downward, represents the center of gravity and shows the os calcis to be off center below the sustentaculum tali, *i.e.*, narrowed on its medial side.

short tendo achillis in case of pain in the calf of the leg. It is of note that cases exist with pronounced deformity without appreciable discomfort to the patient.

Diagnosis—The patient should stand with bare feet, their medial borders held parallel and sufficiently separated to allow a good view between the feet. It will be noted in case of weak feet that the heel bones do not stand erect but incline outwardly from above downward (as viewed from the rear).

The medial borders of the feet are apt to bulge more or less prominently, especially in the vicinity of the scaphoid bone. The longitudinal arch may be depressed to a greater or less degree. The feet may be red and swollen (Figs 2 and 3). Tenderness to pressure over the deltoid ligament, beneath the tip of the lateral malleolus or under the heel bone at the attachment of the plantar fascia or even along this structure, may be elicited. In some cases the peroneal tendons stand out prominently, due to spasm. There may be a limp and the patient often complains of inability to obtain comfortable shoes, a situation due to the feet rather than the shoes. In case of rigid weak foot, there is marked stiffness and loss of suppleness due to concomitant arthritis,

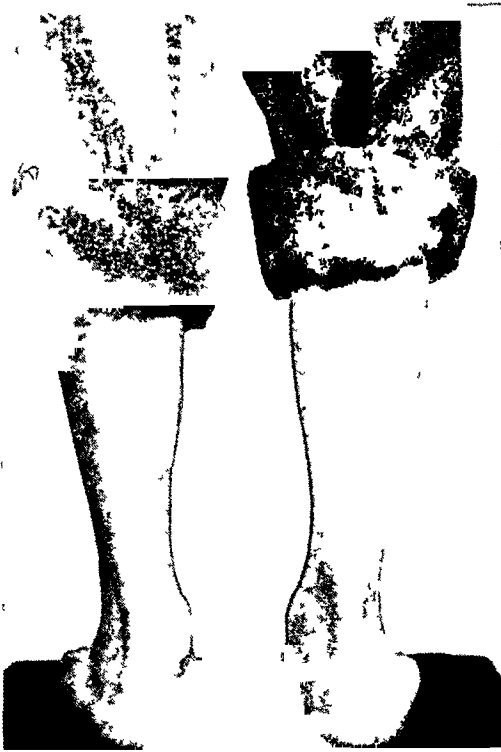


FIG 2—J. L. Case 4. An instance of bilateral flatfoot. Note bulging medial borders of ankles and outward slant of heels.



FIG 3—Same case as Figure 2. Note flatness of longitudinal arch and venous congestion.

either infectious or coming on as a consequence of the prolonged strain of malalignment. Such feet require special treatment not coming within the province of this article.

Treatment—Conservative treatment has been undertaken for a long time but without permanent results—the deformity remains. Strapping of the feet with adhesive plaster, Thomas heels and numerous types of braces, or “arch supports,” have all been used with some success in alleviating or relieving the symptoms. Exercises designed to strengthen the tibial muscles have been emphasized, but no voluntary muscle alone, however strong, will continuously hold firmly against the outward rotation of the foot under weight-bearing.* Many,⁴ the gynecologist, used to tell the class in discussing

* By this, I do not mean to imply that the exercises are not beneficial, only that they do not effect cures *per se*.

perineorrhaphy "The fasciae of the pelvic floor must be brought together and sutured for adequate support of the pelvic organs. One cannot rely upon the muscles of the pelvic floor, for no voluntary muscle will withstand constant strain without fatigue and relaxation. The fasciae, being of connective tissue, will do that." An axiomatic truth is there expressed and holds equally good here.

Author's Operation—A curved incision is made behind and below the internal (medial) malleolus, beginning about one inch above the level of the

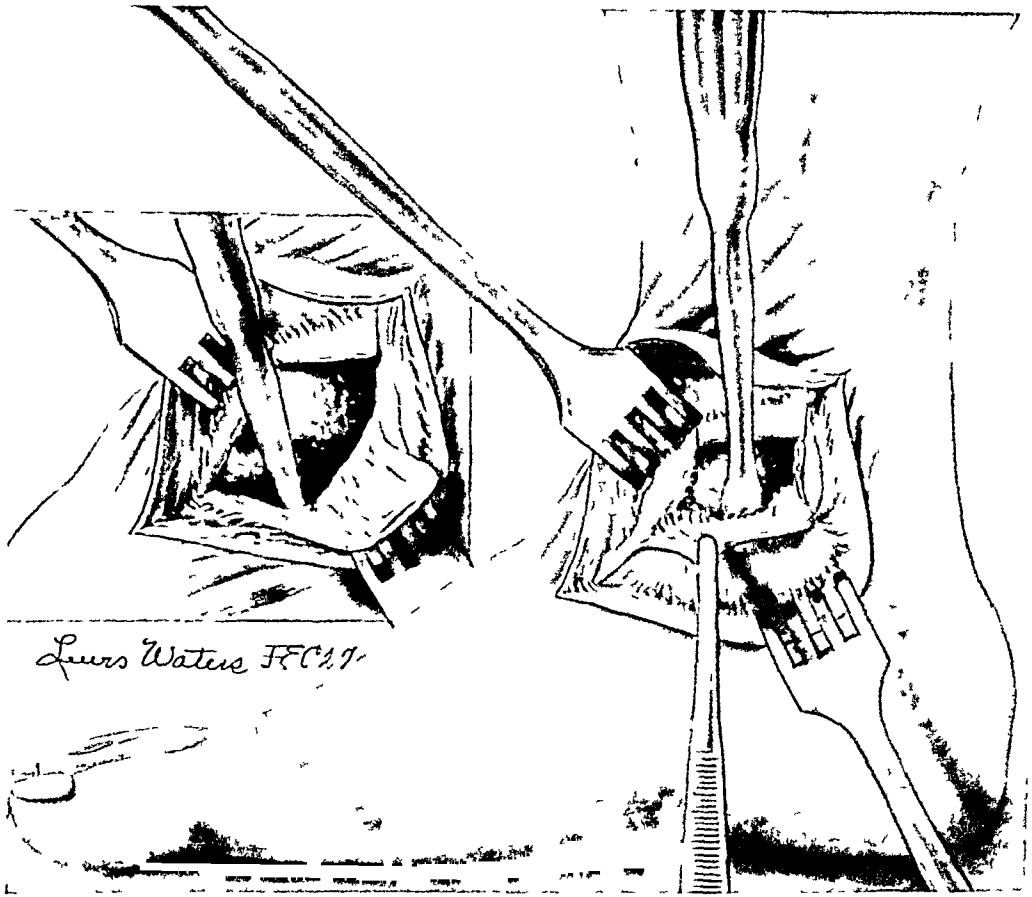


FIG. 4—Author's Operation. Malleolus exposed and dissection of periosteal flap begun. Note tendon of the tibialis posterior undisturbed. Inset: Dissection continued downward stripping the deltoid ligament from the medial malleolus side of astragalus and forward to scaphoid bone. The ankle joint is thus exposed. Note elevation of periosteum above, facilitating later closure.

tip of that bone and midway between the bone and the adjacent margin of the tendo achillis and carried down and forward to the astragaloscaphoid joint (talonavicular). A skin flap is dissected up proximal to this incision in such manner as to uncover the malleolus. With a scalpel, the periosteum is incised transversely to the bone above and vertically from the ends of this incision so as to outline the front and back limits of the malleolus. Care should be taken not to open the sheaths of the tendons behind. From the lower end of the front incision, the soft parts are incised obliquely downward and forward along the anterior margin of the deltoid ligament to the scaphoid bone. A periosteal elevator is now used to free the periosteum from the bone both

FLATFOOT

downward and slightly upward from the transverse incision, this latter to allow easy suturing later on. The dissection of the periosteum is continued downward to pick up the deltoid ligament, freeing it from the malleolus and the medial aspect of the astragalus. The dissection is carried close onto the bone, forward to the scaphoid, downward to the sustentaculum and backward and downward alongside the astragalus*. The elevator must be turned rather vertically in freeing the ligament from the tip of the malleolus, obliquely from that point on. The dissection passes beneath the tendons in this vicinity

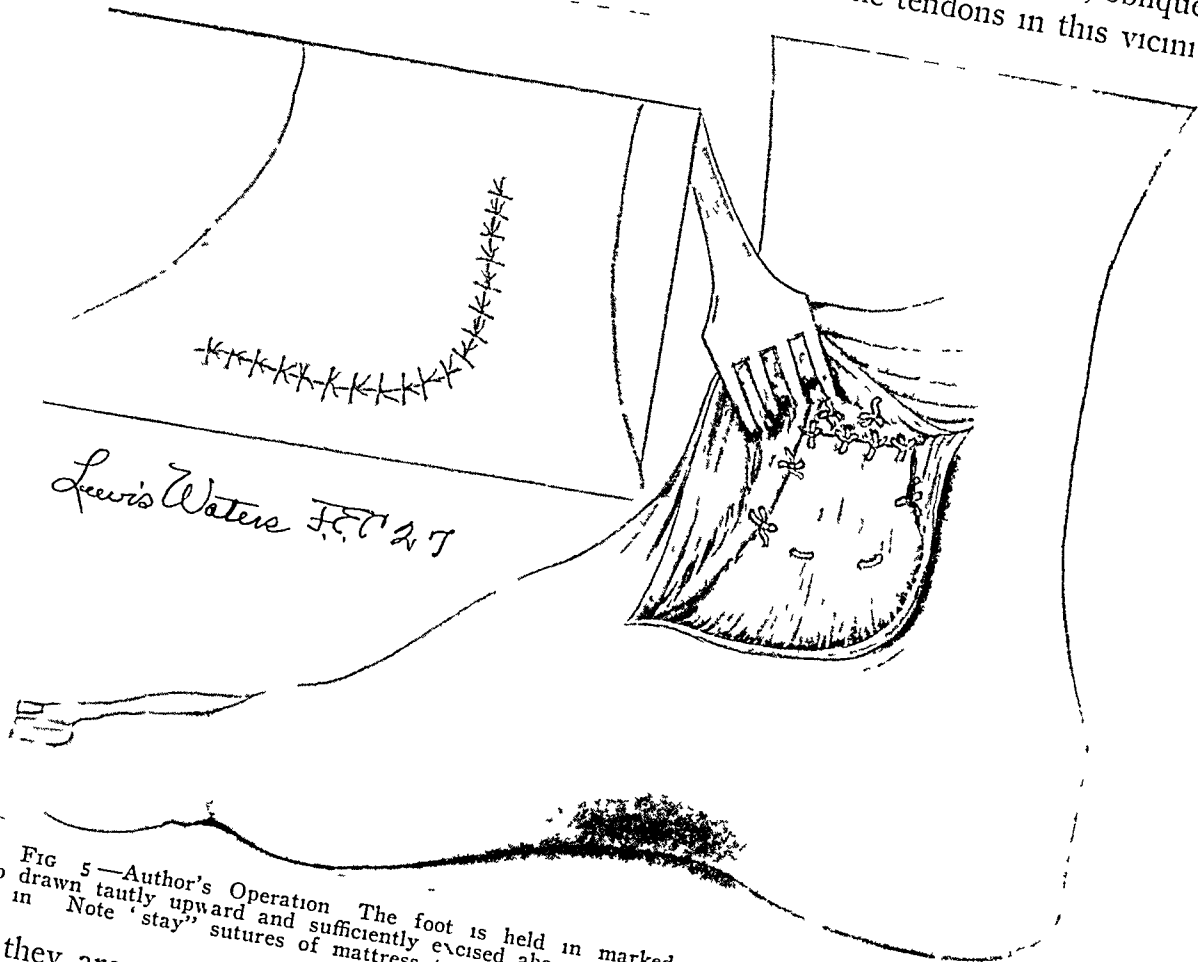


FIG 5—Author's Operation. The foot is held in marked varus, the periosteal ligamentous flap drawn tautly upward and sufficiently excised above to take up the slack. Sutures have been put in. Note "stay" sutures of mattress type. Inset: Skin incision as closed.

and they are returned undamaged to their normal relationships in closure. The deltoid ligament is now free down to its distal fan-shaped insertion (Fig 4). An assistant now holds the foot in a marked varus attitude with special attention to the heel. Tension upward is put upon the periosteal-ligamentous flap and this is excised above to the extent that it overlaps the transverse periosteal incision. Chromic gut or kangaroo tendon is used to suture the flap above and at its sides but it is well to place a few deep "stay" sutures, of mattress type, through the thick part of the deltoid to be attached above as a preliminary. The skin may be closed with dermal sutures (Fig 5). If the tendo achillis is too short, it should be elongated by the "Z-method" as a pre-

* A slight flow of synovial fluid will indicate exposure of the joints

TABLE I
SUMMARY OF EXPERIENCE WITH OPERATION

Case	Patient	Age	Sex	Nationality	Date of Oper's	No of Oper's	Last Exam	Results	
								Clinical	Deformity
1	W T	18	M	White American	{ Rt, Dec 13, 1926 Lt, Apr 11, 1927	2	April, 1938	Good	Corrected
2	J G C	30	M	Mexican	June 29, 1927	2	Dec, 1927	Good	Corrected
3	J T	18	M	White American	{ Lt, Feb 15, 1928 Rt, June 27, 1928	2	April, 1930	Good	Corrected
4	J L	30	M	Hebrew	April 25, 1928	2	Jan 10, 1939	Good	Corrected
5	R C M	11	M	White American	Nov 16, 1929	2	Jan, 1938	Good	Corrected
6	C B B	3	M	White American	Feb 22, 1930	2	1937	Good	Corrected
7	H G G, Jr	6½	M	White American	July 29, 1930	2	Jan, 1938	Good	Corrected
8	L M A	12	F	White American	July 29, 1930	2	Jan, 1939	Good	Corrected
9	J E	22	F	German	July 22, 1931	2	Oct 21, 1938	{ Rt Good Lt Poor	Corrected Recurred*
10	E H	6	F	White American	Sept 3, 1932	2	Oct 28, 1938	{ Lt Good Rt Fair	Corrected Partial recurrence†
11	G B	12	M	White American	Mar 4, 1936	1	Oct 29, 1938	Poor	Recurrence†
12	A A	34	M	Negro	July 15, 1936	1	Oct 24, 1938	Good	Partial recurrence*
13	W L	22	M	Negro	April 7, 1937	2	Nov 1, 1938	{ Rt Good Lt Pain*	Corrected Corrected
14	L F	39	M	Negro	July 12, 1937	1	Dec 20, 1938	Good	Corrected
Total						—	25†		

* These patients had periostitis, etc., of gonorrheal origin

† These patients showed poor cooperation in after-care

‡ This does not represent all of the cases operated upon, only those on whom results could be traced

liminary A plaster-of-paris bandage is applied over the sterile dressings, extending from the toe tips nearly to the knee. Naturally, the foot and heel must be held firmly in inversion or varus until the plaster has become firm.

Postoperative Care—Upon completion of the operation, the foot appears to have a varus deformity and the same is true upon removal of the plaster bandage some weeks later, but this need cause no concern, as it will soon regain its normal appearance and must, in fact, be protected against undue strain lest a recurrence of the deformity take place after the removal of the plaster bandage. For that purpose, adhesive plaster strapping may be used until the

FIG 6

FIG 7

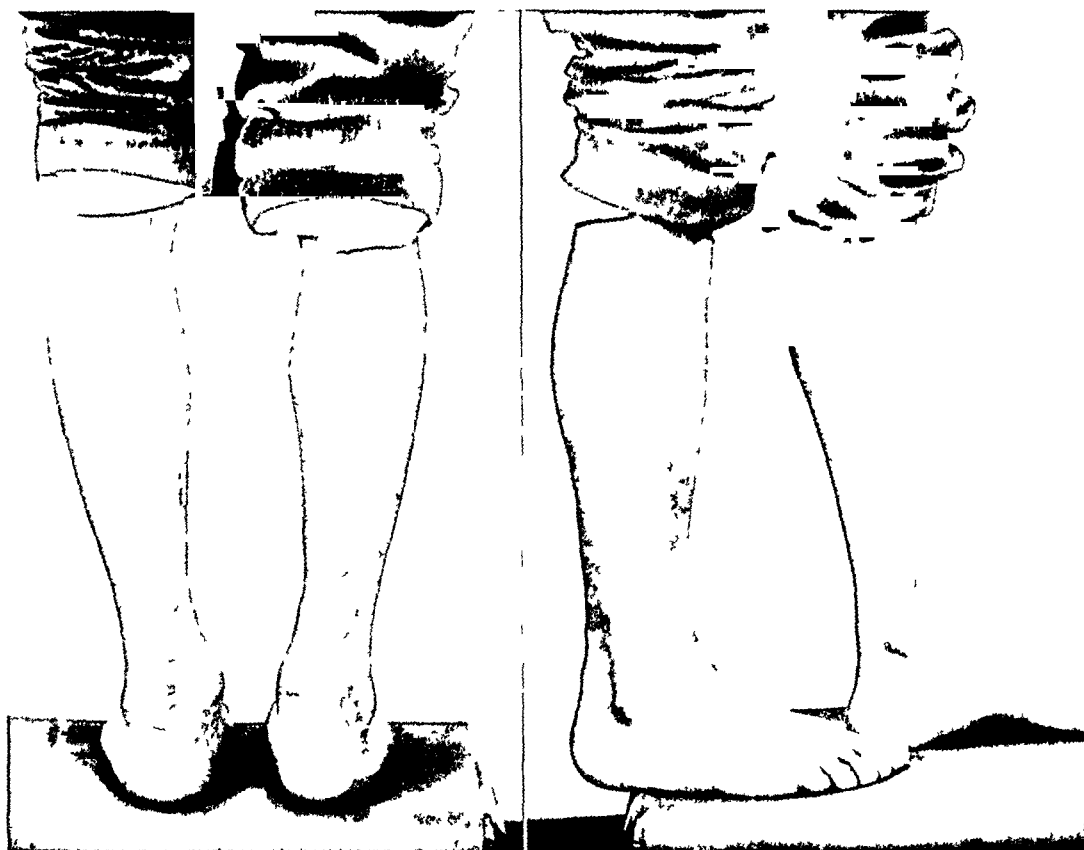


FIG 6—Case 2. Postoperative result at the end of six months. Note vertical attitude of the heels.

FIG 7—Same patient as in Figure 6. Operated upon in 1927, showing the result six months postoperative. Note longitudinal arch is restored in left foot. Plaster casts of feet before and after operation show not only correction of extreme deformity but shortening of medial borders of feet as well.

tenderness has lessened following removal of the sutures. Thomas heels or braces (or both) are used to raise the medial sides of the heels when the patient begins to walk. The weight must be kept off the feet for at least five or six weeks following operation. During that period, the patient may sit up, get about in a wheel-chair or be transported in an automobile. But time must be allowed for firm union of the ligament to the bones to occur before the patient is allowed to stand or walk without adequate support.* Of course, if

* This support should be kept up for at least six months. This is very important to success.

FIG 8

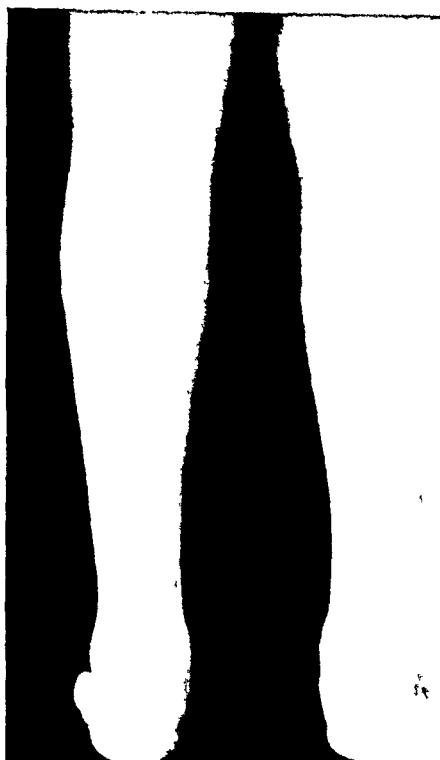


FIG 9



FIG 8—Case 7 Postoperative results after seven and one half years. Note excellent alignment of feet and absence of bulging on medial sides of ankles

FIG 9—Same patient as in Figure 8. Showing a good longitudinal arch on the right foot and a correct alignment of the left foot

FIG 10



FIG 11



FIG 10—Case 5 Postoperative result after eight years. Note the vertical attitude of the heels with absence of bulging in the scaphoid regions

FIG 11—Same patient as in Figure 10. Note the excellent restoration of the longitudinal arch of the right foot, and the correct alignment of left foot

only one foot at a time is operated upon, crutches may be used and the patient made ambulatory

Since 1926, the author has performed 25 of these operations, a sufficient length of time having elapsed, therefore, to afford a test of the durability of the results (Table I) Some of the patients have been lost sight of, largely through moving to distant points, but great effort has been made to ascertain their present status, if they could be found Recurrence of deformity, either partial or complete, has not been frequent It is chargeable to poor cooperation in after-care or subsequent development of inflammatory disturbance of gonorrheal origin in some of the adults The existence of calcaneal "spurs" in these latter is highly suggestive as to the source of trouble A low state of nutrition in some of the younger patients may have been a factor The majority of patients have been from charity clinics, hence the presence of such obstacles to success is easily explainable The ages of the patients have ranged from three to 39 In the youngest case, the separation of the flap was difficult on account of the great softness of the bones For that reason, it is perhaps better to wait until the patient has reached the age of six or eight

Any opinion expressed by the writer would be purely personal as to the effectiveness of this procedure, but it is his belief that, when it is carried out properly on well selected cases, the results both clinically and anatomically will be highly satisfactory in the majority of cases

In three operations, the technic was modified to include an arthrodesis of the astragaloscaphoid joint of one foot, and a shortening of the plantar fascia by imbrication through a transverse incision in both feet of another patient The results in those patients did not appear to warrant the additional procedure, and the operation as above described has been used exclusively within recent years

CONCLUSIONS

(1) Flatfoot is the direct consequence of a deltoid ligament too long to perform its normal function of holding the os calcis in the erect attitude during weight-bearing

(2) The valgus attitude, or outward slanting of the heel, is the only constant, appreciable objective sign

(3) Early fatigue is the one constant, subjective symptom

(4) Palliative measures may relieve symptoms but do not effect cures

(5) Restoration to normal can be attained only by attacking the problem at its source—the deltoid ligament must be shortened surgically

(6) The operation is adequate, because it utilizes the normal anatomy of the foot in correcting the deformity No joints are destroyed by arthrodesis as has been done in practically all of the operations heretofore reported

* It will be noted that throughout this discussion, the height of the longitudinal arch is not stressed, this factor being regarded as of secondary importance and having no real value in the cause of the pathology

REFERENCES

- ¹ Schoolfield, Ben L. An Original Operation. *Dallas Med Jour*, 14, No. 2, 17-18, February, 1928
- Wallace, Charlton. Personal communication
- Schoolfield, Ben L. Report of a Case of Bilateral Relaxation of the Superior Tibio-fibular Articulation. *Jour Bone and Joint Surg*, 9, No. 3, 500-501, July, 1927
- ² Roberts, Percy Willard. The Initial Strain in Weak Foot. *New York Med Jour*, 102, 441, August 28, 1915
- Idem*. Prevention and Treatment of Weak-Foot in Children. *J A M A*, 75, 237-240, July 24, 1920
- ³ Maury, John Metcalfe. Former Professor of Gynecology, University of Tennessee, College of Medicine, Memphis, Tenn. Personal communication

THE TREATMENT OF ANKLE MALUNION

A STUDY OF END-RESULTS

WILLIAM R. HAMSA, M.D.

OMAHA, NEB.

FROM THE UNIVERSITY OF IOWA, DEPARTMENT OF ORTHOPEDICS, SERVICE OF DR. ARTHUR STEINDLER

THE TRAUMA and strain of weight-bearing place great stresses upon the articular and periarticular structures of the lower extremities. Thus, minor joint incongruities which would be considered negligible in the joints of the upper extremity are sufficient in the lower extremities to produce unfavorable results over a longer period of time. This is especially true of the ankle joint, where the synchronization of motion between the tibiofibular mortise, the astragalus, and subastragaloid joint is marked. This latitude of motion may be a predisposing factor to the frequent ankle disability with which we are at present concerned, namely, the fractured ankle. Malunion following the usual Potts or Cotton fracture occurs frequently even in the hands of those experienced in approved methods of treatment of these fractures. Failure of immediate or early closed reduction of a fracture is usually followed by necessity for open operation, either immediate, to properly repose the fragments, or late, to reconstruct the joint which has progressed to the stage of degenerative arthritis with associated disability consisting of pain, weakness and instability.

Treatment of these unfavorable end-results may be either conservative or operative. The former, and incidentally the initial method in the majority of cases, consists of support in the form of inner-wedged shoes, arch supports, elastic bandaging, braces, physiotherapy, such as heat, massage and contrast baths, and medication in the form of salicylates. Suggestive arthritic histories are always followed by appropriate investigations for possible foci of infection and their eradication.

Conservative therapy failing, surgical correction of malunion or of traumatic sequelae is necessary. Accurate apposition of fragments, however, is difficult and can be successful only in very early stages, apposition in the late stages is associated with sufficient operative trauma to instigate traumatic arthritic changes. Other methods of attack are, therefore, necessary. Malunion is often associated with considerable disalignment and the correction of this deviation responds favorably to an osteotomy properly placed (Fig. 1). Astragalectomy may place the weight-bearing stresses in a more favorable region, especially if both tibio-astragaloid and subastragaloid joints had been involved in the fracture (Fig. 2). The foot may be stabilized and aligned by an arthrodesis of subastragaloid and midtarsal joints if these had been injured, but this procedure overlooks the ankle joint proper which is

usually altered as well (Fig 3) Ununited fragments may be excised when they serve as a block to free motion provided their absence will not decrease the stability of the angle (Fig 4) Lastly, the tibio-astragaloid joint may be obliterated surgically as well as the subastragaloid and midtarsal joints¹

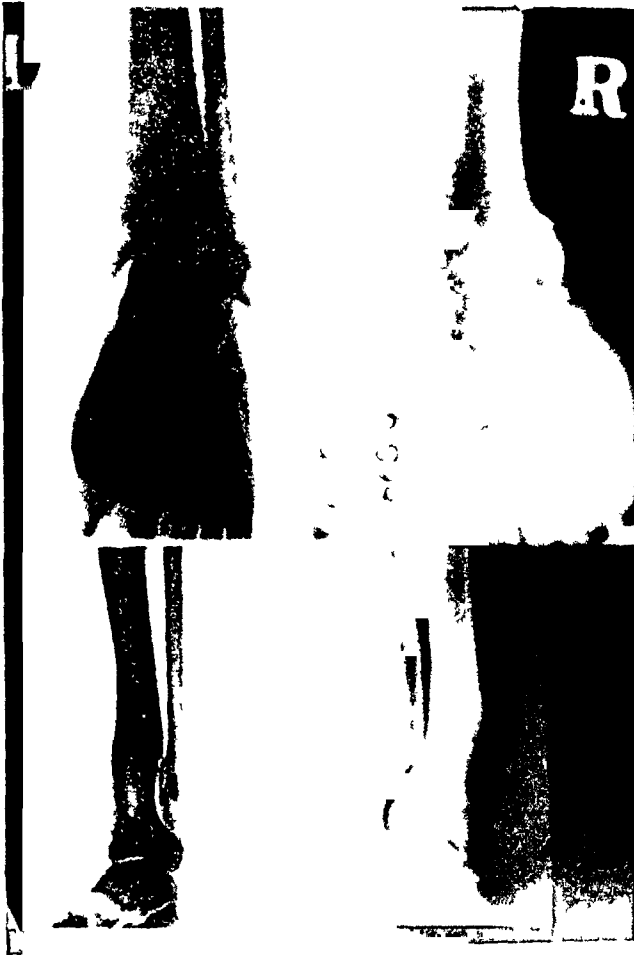


FIG 1—Supramalleolar osteotomy for ankle varus



FIG 2—Astraglectomy

(Fig 5) Fusion of the tibio-astragaloid joint alone in ten to 15 degrees equinus produces a fairly movable foot as compensatory increase in motion follows in the subastragaloid and midtarsal joints Fusion of all the joints about the astragalus produces a stable and painless foot, the gait being but little disturbed (Fig 6)

ANKLE MALUNION



FIG 3—Triple arthrodesis for old fracture of the astragalus with traumatic arthritis of the subastragalal joint

FIG 4—Fracture of Stieda's process of the astragalus, relieved by surgical removal of the fragment



FIG 5—Tibioastragalar arthrodesis for old fracture of the posterior margin of the tibial joint surface, with traumatic arthritis

Material for this study consists of 113 patients seen on the Orthopedic Department at the State University of Iowa. These malunions are divided according to pathology present: Supramalleolar 16, bimalleolar 47, malleolar with rupture of lower tibiofibular ligaments 11, trimalleolar 11, astragalus 28. With little difficulty, these may easily be placed in the grouping suggested by Ashhurst.² For technique, the reader is referred to any standard operative orthopedic procedure.³



FIG 6—Pan-astragloid arthrodesis for old severe fracture of the ankle

Results are classified as follows:

- (1) Good—stable, painless weight-bearing, in surgical group, no support
- (2) Fair—functioning foot with occasional slight discomfort, in surgical group, no support
- (3) Poor—continuance of same or allied symptoms

SUPRAMALLEOLAR TIBIAL AND FIBULAR MALUNIONS

Conservative treatment was used in seven cases: males five, females two, ages ranging from 21 to 71 years, average 42 years. Results were as follows:

Good—None

Fair—5, injury average, 28 yrs, observed average, 62 yrs

Deviation—varus 3, valgus 1, anterior bow 1

Poor—2, injury average, 15 yrs, observed average, 25 yrs

Deviation—varus 1

ANKLE MALUNION

Surgical treatment was resorted to in nine cases males seven, females two, ages ranging from seven to 50 years, average 32 years Results were as follows

Good—5, injury average, 13 yrs, observed average, 2 yrs
3 osteotomies, tibia and fibula for deviation, varus 1, valgus 1, anterior bow 1
1 osteomyelitis drainage with final spontaneous panastragaloid fusion
1 triple arthrodesis for fracture os calcis with slight supramalleolar varus

Fair—3, injury average, 19 yrs, observed average, 42 yrs
1 supramalleolar osteotomy and subsequent tibio-astragaloid arthrodesis, subsequent mild subastragaloid arthritis
1 supramalleolar osteotomy, later mild ankle arthritis
1 panastragaloid arthrodesis, subsequent infection, relieved, some persistent swelling of foot

Poor—1, amputation, midleg

Of the conservatively treated patients, the chief difficulty was the arthritic pain on prolonged use Support of any type is only palliative and moderately efficient The best solution in this traumatic arthritic group is the arthrodesis as exemplified by the responses in the three patients treated surgically in this manner The supramalleolar osteotomy for realignment is successful only when the normal relationship between articular surfaces of the tibia and astragalus have not been materially changed, any evidence of traumatic arthritis should speak for arthrodesis The only amputation performed followed severe circulatory disturbance after a supramalleolar osteotomy for a severe valgus deformity

BIMALLEOLAR FRACTURE MALUNIONS

Conservative treatment was used in 31 cases, males 16, females 15, ages ranging from 14 to 74 years, average 46 years Results were as follows

Good—None

Fair—22 injury average, 3 yrs, observed average, 41 yrs
Deviations—valgus 12, varus 4

Poor—9, injury average, 67 yrs, observed average, 41 yrs
Deviations—valgus 3, varus 2

Surgical treatment was resorted to in 29 cases males 20, females nine, ages ranging from 13 to 69 years, average 37 3 years Results were as follows

Good—12, injury average, 14 yrs, observed average, 4 yrs
1 manipulation and cast for valgus foot and ankle in a male, age 13
1 triple arthrodesis for associated fracture astragaloid head and neck
2 osteotomies, malleolar, with bone graft
6 panastragaloid arthrodeses for pantraumatic arthritis (1 bilateral)
3 osteomyelitis drainages with spontaneous panastragaloid fusion

Fair—7, injury average, 6 yrs, observed average 42 yrs

- 1 removal chip fracture internal malleolus, subsequent arthritis
- 2 triple arthrodeses for associated fracture astragalar neck
- 4 osteotomies, 1 associated reconstruction internal malleolus

Poor—10, injury average, 18 yrs, observed average, 63 yrs

- 1 manipulation and cast for valgus foot and ankle in a male, age 69
- 4 removal chip fractures, 3 severe arthritis, 1 severe osteomyelitis and loss of leg
- 1 osteotomy supramalleolar for varus, arthritis increased
- 4 amputations for severe malunion, osteomyelitis and circulatory deficiency

Especially when deviation of any type was present, this malunion has disturbed the normal relationship between the tibia and astragalus. The favorable end-results of surgical therapy are therefore, represented by nine joint arthrodeses for degenerative changes. Further, three osteomyelitis drainages eventually led to a result equivalent to an operative arthrodesis but with fusion of more joints than would have been fused had reconstruction been performed. The inadequacy of forceful manipulations for deformity in old individuals is illustrated.

MALLEOLAR MALUNIONS WITH RUPTURE OF LOWER TIBIOFIBULAR LIGAMENTS

Conservative treatment was used in seven cases—males four, females three, ages ranging from 20 to 64 years, average 42.4 years. Results were as follows:

- Good—1, injury 9 yrs old, observed 2 yrs, brace 3 mos, complete relief, roentgenogram, mild traumatic arthritis of ankle
- Fair—4, injury average, 12 yrs, observed average, 13 yrs, all in slight valgus
- Poor—2, injury average, 11 yrs, observed average, 15 yrs, marked traumatic arthritic changes, both in valgus

Surgical treatment was resorted to in four cases—males one, females three, ages ranging from 29 to 55 years, average 39.7 years. Results were as follows:

- Good—2, injury average, 22 yrs, observed average, 6 yrs
 - 1 supramalleolar osteotomy for varus
 - 1 supramalleolar osteotomy, subsequent panastragaloid arthrodesis, for valgus
- Fair—None
- Poor—2, injury average, 09 yrs, observed average, 16 yrs
 - Fibular osteotomies and forceful replacement astragalus, resultant marked arthritic changes

The similarity of this group to the preceding is noted. When diastasis of the ankle mortise is marked, simple realignment proves inadequate, joint obliteration being necessary, if associated arthritic changes are not present at that time, they are certain to develop within a relatively short period of time.

ANKLE MALUNION

TRIMALLEOLAR FRACTURE MALUNIONS

Conservative treatment was used in five cases males two, females three, ages ranging from 17 to 58 years, average 47.8 years. Results were as follows

Good—1, injury 3 mos. old, observed 2 yrs., brace for 3 mos.

Fair—3, injury average, 5 mos., observed average, 12 yrs., valgus in all, braces necessary

Poor—1, injury 5 yrs. old, observed 1 yr., marked arthritis with pain

Surgical treatment was resorted to in six cases males two, females four, ages ranging from 25 to 55 years, average 44.1 years. Results were as follows

Good—None

Fair—4, injury average, 16 yrs., observed average, 18 yrs.

2 tibio-astragaloid fusions, later mild subastragalar arthritis

1 bone graft and tendo achillis lengthening, mild ankle arthritis

1 astragalectomy, slight discomfort if too active

Poor—2, injury average, 9 mos., observed average, 5 yrs.

1 tibio-astragaloid fusion, later severe subastragalar and midtarsal arthritis

1 panastragaloid fusion, later repeated for failure, later developing severe circulatory difficulty not responding to sympathectomy

Conservative treatment with brace support relieved a good portion of patients, doubtless because of the indirect limitation of motion. The surgical results are mediocre only, the fusions performed were no doubt adequate for the joint obliterated but the subsequent appearance of similar symptoms in remaining tarsal joints produced failures. Can these failures be due to arthrodesis, that is not sufficiently radical to remove all arthritic locations?

ASTRAGALUS FRACTURE

Fracture Astragalar Head—Conservative treatment was used in six cases males four, females one, ages ranging from 13 to 53 years, average 34 years. Results were as follows

Good—None

Fair—3, injury average, 14 mos., observed average, 6 mos., arthritic complaint if too active on rough ground

Poor—3, injury average, 15 yrs., observed average, 5 yrs., pain in foot on any walking, support necessary

Surgical treatment was resorted to in two cases male one, female one, age being 20 and 24 years. Results were as follows

Good—2, injury average, 2 yrs., observed average, 5.5 yrs.

1 triple arthrodesis

1 astragaloscaphoid arthrodesis

Fracture Astragalar Body—Conservative treatment was used in eight cases males five, females three, ages ranging from 19 to 74 years, average 51 years. Results were as follows

- Good—2, injury average, 4 yrs, observed average, 15 yrs, both chip fractures medial or lateral articular edge
- Fair—4, injury average, 4 yrs, observed average, 17 yrs, 2 crush fractures, 1 chip fracture, 1 laterally, 1 medially 1 associated fracture anterior tibial margin
- Poor—2, injury average, 27 yrs, observed average, 35 yrs Both fractures at junction body and neck, previously well reduced by open operation 1 poor open reduction previously with osteomyelitis

Operative intervention in nine cases males seven, females two, ages 23 to 52 years, average 35 years, showed the following results

- Good—7, injury average 5 yrs, observed average, 55 yrs, 4 astragalectomies, 2 supramalleolar osteotomies with ankle fusion, 1 triple arthrodesis
- Fair—1, injury 9 mos old, observed 9 yrs, triple arthrodesis, arthritic history
- Poor—1, injury 9 yrs old, observed 8 yrs, astragalectomy, good result for 25 yrs when arthritic changes developed

Fracture of Stieda's Process of Astragalus—Conservative treatment in three cases, all males, ages seven to 34 years, average 27 years, showed the following results

Good—None

Fair—1, injury 2 yrs old, observed 6 mos, subastragalar joint arthritis, mild

Poor—2, injury average, 1 yr, observed average, 3 yrs, subastragalar joint arthritis, severe

Surgical treatment in one case, a male, age 18, injury 3 mos old, observed 4 yrs, produced a good result following removal of the fragment

An obvious conclusion from all old talar fractures treated is that the surgical obliteration of involved joints produced the best results. The good result following removal of the posterior process chip fracture may be explained on the basis of early intervention. Considerable argument arises relative to choice between astragalectomy and arthrodesis for body fractures, a sane attitude is the choice of panastragaloid fusion if blood supply is adequate—otherwise total removal of the astragalus rather than partial removal should follow

CONCLUSIONS

(1) A large number of ankle malunions respond to conservative methods, as modeled insoles, brace supports and physiotherapy

(2) When the relationship of tibial and astragaloid joint surfaces has been undisturbed, even in the face of deviation above the joint, conservative operation, as an osteotomy, aimed at realignment and carefully performed in the supramalleolar region, serves as an efficient procedure, should this relationship be altered, the same procedure is doomed to failure, as the pain due to arthritic changes will continue or will appear at some subsequent time, this type of disorder responds only to a joint arthrodesis

(3) Early arthrodesis is indicated in any ankle fracture in which the

joint surfaces show incomplete reduction, a subsequent arthrodesis is in order for any malunion which has not responded to a more conservative procedure

(4) In reconstructing an ankle malunion, it is better to arthrodesis all joints with suspicious arthritic changes even though a panastagaloid fusion follows, this prevents possible continuation of pain due to arthritic changes in previously unsuspected joints, function of such a fused foot is efficient, stable, and painless, as the ten to 15 degree equinus is compensated for by the ordinary shoe heel

REFERENCES

- ¹ Speed, J S, and Boyd, H B Operative Reconstruction of Malunited Fractures About the Ankle Joint Jour Bone and Joint Surg, 18, 270, April, 1936
- ² Ashhurst, A P C, and Bromer, R S Classification of Ankle Fractures Arch Surg, 4, 51, 1922
- ³ Steindler, Arthur A Textbook of Operative Orthopedics, D Appleton Co, New York, 1925

BRIEF COMMUNICATIONS AND CASE REPORTS

HERNIA THROUGH THE TRANSVERSE MESOCOLON AND THE GASTROCOLIC OMENTUM*

REPORT OF A CASE FOLLOWING POSTERIOR GASTROJEJUNOSTOMY

HAROLD J. SHELLEY, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE AND GASTRO-INTESTINAL CLINIC, ST. LUKE'S HOSPITAL, NEW YORK CITY, N. Y.

HERNIATION of the small intestine through the transverse mesocolon into the lesser peritoneal sac was evidently a fairly common occurrence early in the history of posterior gastro-enterostomy. This is indicated, not by their frequent reports in the literature of that period, but by the fact that in such a large proportion of the descriptions of the technic of the operation one is cautioned to close the opening in the transverse mesocolon as, otherwise, this accident so frequently occurs. In a search for reports of this type of hernia only two were found. Moynihan,¹ in 1912, in his book on duodenal ulcer, described two cases both were herniae of the small intestine into the lesser sac. One patient died, the other survived, following operative reduction of the hernia.

Intra-abdominal herniae of the small intestine passing behind the afferent loop of jejunum have been reported 15 or more times. Hernia of the small intestine through a congenital opening in the transverse mesocolon (or through an opening produced in some manner not associated with any operation) has been reported one or more times nearly every year for the past several years.

Case Report—Hosp. No. 118-289. M. M., white, male, age 38, was admitted to St. Luke's Hospital October 5, 1936. Ten months previously, because of pain in the right epigastrium, nausea and vomiting and a pyloric stenosis, demonstrated by fluoroscopic examination, a posterior gastrojejunostomy had been performed at another hospital. For the first two months following this operation the patient was on ambulatory medical ulcer treatment and remained free from symptoms. One month after he returned to an unrestricted diet, he began to notice a pain similar to that which he had had before the operation, but which was now situated just above and to the left of the umbilicus. He had attacks of nausea but did not vomit. The pain was of a dull, gnawing character, fairly constant, did not radiate, and was not relieved by alkalis. At times it was partially relieved by food and at other times aggravated. His stools were in the majority black, but not described as tarry. In the St. Luke's Hospital, Gastro-Intestinal Clinic, he had been placed on an ambulatory ulcer treatment without relief.

Physical Examination—The patient was poorly nourished, but otherwise negative except for a well healed transverse, upper, midabdominal scar and tenderness to pressure immediately above and to the left of the umbilicus.

* Presented before the Surgical Section of the New York Academy of Medicine, December 3, 1937. Submitted for publication, June 6, 1938.

Laboratory Data—An alcohol test meal showed free hydrochloric acid 18, total acidity 38. Guaiac examination of the stool for occult blood was negative on four occasions. The blood Wassermann test was negative.

Röntgenologic Examination—A marked irregularity was demonstrated and tenderness elicited at the site of the gastrojejunostomy stoma, which at first appearance suggested new growth about the stoma, but also one that might well have been produced by a marginal ulcer and spasm. There was essentially no emptying through the pylorus (Fig 1).

Treatment—An 18-day medical ulcer regimen, with the patient in bed, gave relief from the pain, although a subsequent gastro-intestinal series still showed some spasm of the gastrojejunostomy stoma.



FIG 1—Roentgenogram of a gastro-intestinal series taken on October 6, 1936. There is practically no emptying through the pylorus. The filling defect about the gastrojejunostomy stoma can be readily seen.



FIG 2—Roentgenogram of a gastro-intestinal series taken on May 27, 1937. There is still practically no emptying through the pylorus. The dilated loops of small intestine can be seen. Some of these lie up against the greater curvature of the stomach. The large filling defect about the stoma is no longer present.

He was then discharged to the Gastro-Intestinal Clinic, where he was cared for during the following seven months' period. Within six weeks of his discharge from the hospital, while on an hyperacidity diet and alkalis after his meals, the symptoms recurred exactly as before admission. Pain and nausea were again present without vomiting or tarry stools. Ambulatory medical treatment gave no relief. Taking food in any form aggravated the pain, which after a few weeks became practically constant.

On May 24, 1937, he was readmitted to the hospital. Three days later a gastro-intestinal series showed tenderness and spasm at the site of the gastrojejunostomy stoma, with still practically no emptying through the pylorus. The loops of small intestine were moderately dilated and some of these loops were situated as high as the greater curvature of the stomach (Fig 2). On a medical ulcer regimen, in bed, he was relieved of his pain, but as soon as he was placed on a convalescent ulcer diet and permitted out of bed, the pain recurred. This management was tried three times more, each time with the same result.

On ten occasions, in the three months of treatment, the stools were positive for blood with the guaiac test, the remaining tests having been negative. An alcohol test

meal gave free hydrochloric acid 14, total acidity 39 *Preoperative Diagnosis* Marginal ulcer and pyloric stenosis

Operation and Operative Pathology—August 16, 1937 Under ether anesthesia, an

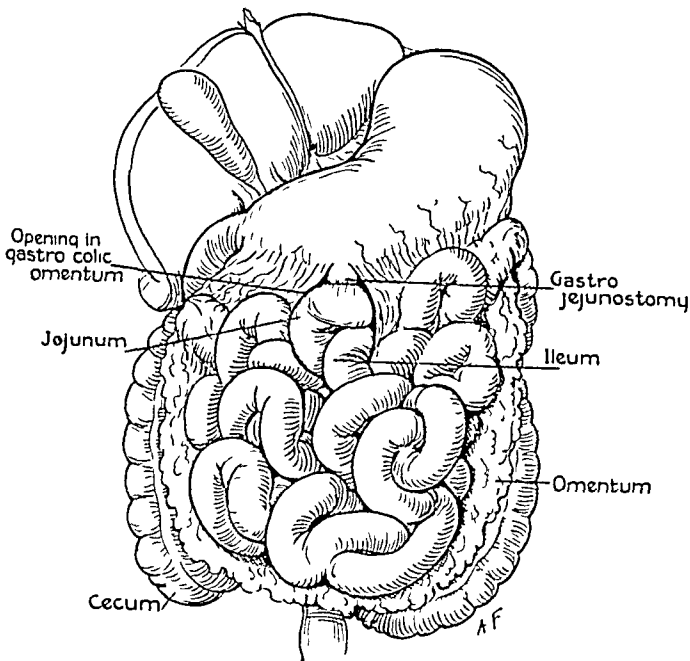


FIG 3—A semidiagrammatic sketch of the condition which presented upon opening the abdomen. The gastrojejunostomy can be seen. The transverse colon and great omentum are covered by loops of small intestine. The component parts of the gastrojejunostomy and the loops of small intestine are herniated through the opening in the transverse mesocolon.

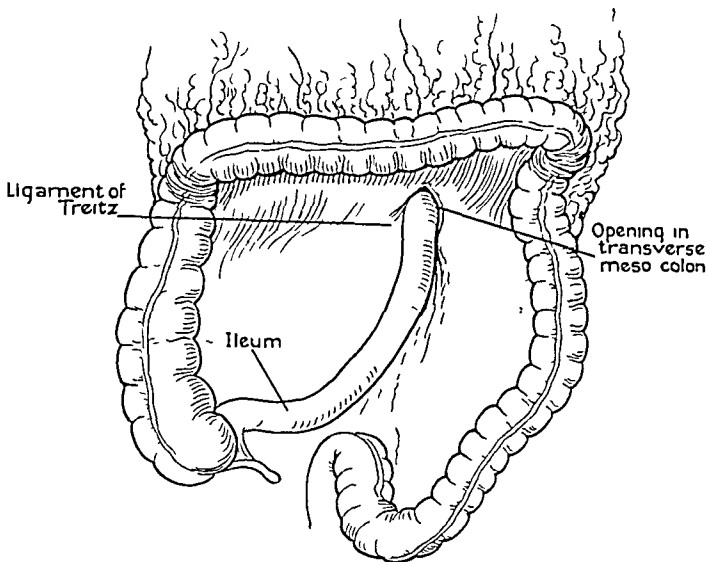


FIG 4—A semidiagrammatic sketch of the conditions as they were found upon turning up the great omentum, the transverse colon and the loops of small intestine which lay in front of these two structures. The small amount of ileum which lay in a relatively normal location can be seen.

upper left rectus incision disclosed numerous adhesions throughout the upper abdomen. When these were freed, the site of the gastro-enterostomy presented, and at first appeared to be of the anterior type. The transverse colon and the greater omentum were entirely

INTERNAL HERNIAE

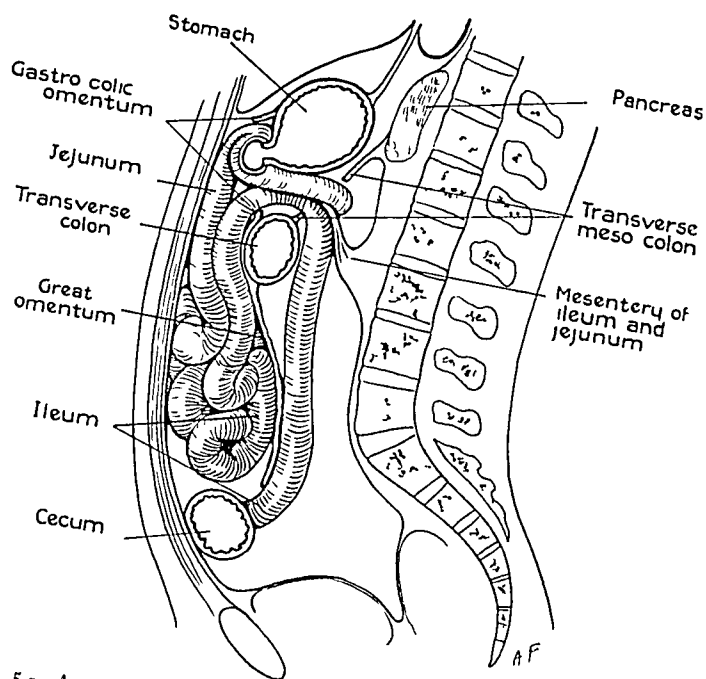


FIG 5—A diagrammatic representation of the condition found at operation. The abdomen is represented in anteroposterior cross section. Naturally some parts of the sketch are shown out of proportion. The relation of the hernia to the various structures in the abdomen can be readily seen. The opening in the gastrocolic omentum is shown much larger than it was in relation to the other structures but this was necessary in order to show which structures passed through it.

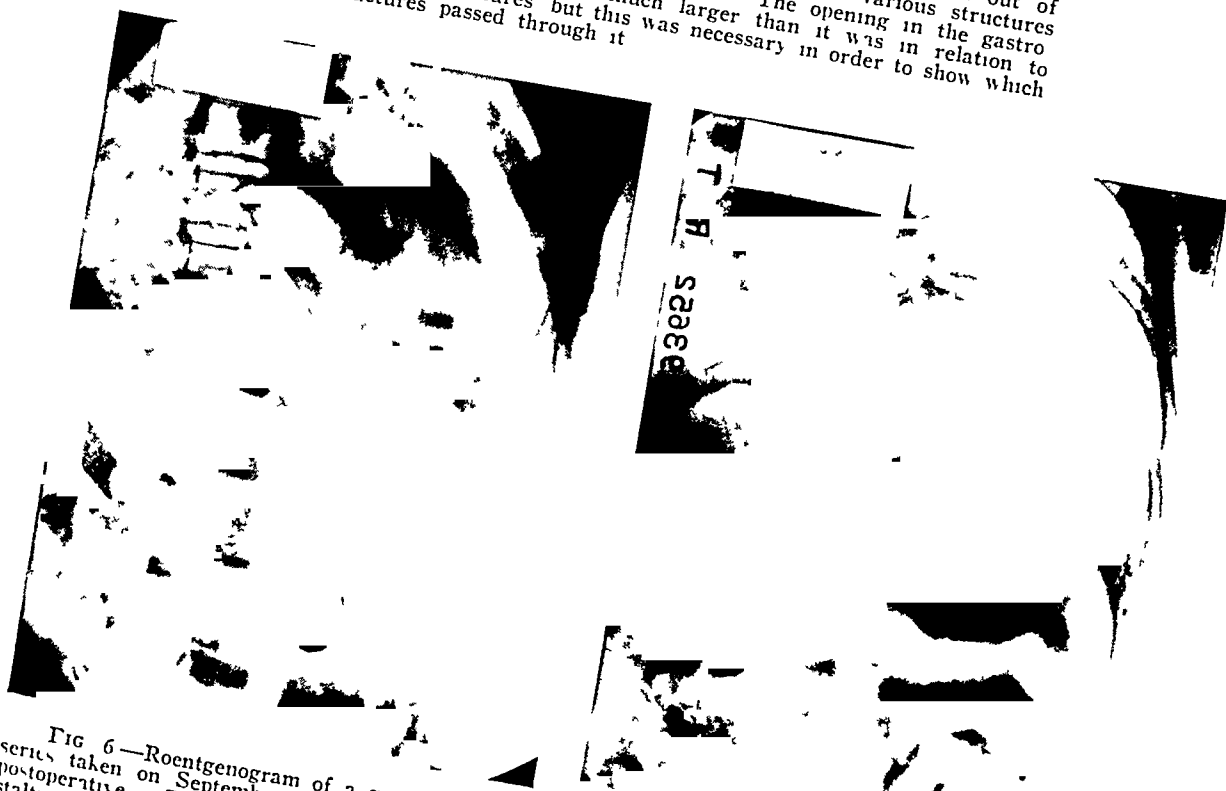


FIG 6—Roentgenogram of a gastroenterostomy series taken on September 13, 1937, four weeks postoperative. The stomach with normal peristaltic waves and normal emptying through a slightly irregular cap can be seen.

FIG 7—Roentgenogram also taken four weeks postoperative. The normal distance between the loops of small intestine and the greater curvature of the stomach can be noted. The loops of small intestine are no longer dilated. The stomach emptied completely within normal limits of time.

covered by loops of small intestine (Fig 3) Upon further examination, it became evident that the entire small intestine from the gastrojejunostomy, which was actually of the posterior short loop type, to within four inches of the ileocecal valve (and including the component parts of the gastrojejunostomy) was herniated through an opening in the transverse mesocolon, across the lesser sac and through an opening in the gastrocolic omentum (Figs 4 and 5) The two openings each admitted three fingers The gastrojejunostomy stoma admitted two fingers readily and about it was only moderate induration The pylorus would not admit the tip of a finger, being stenosed by the scar of a well healed ulcer The loops of small intestine were dilated and their walls hypertrophied, being two to three times the normal thickness

The small intestine and the gastrojejunostomy were reduced through the openings in the gastrocolic omentum and the transverse mesocolon The gastrojejunostomy was taken down, including an excision of the entire margin of the stoma This area was indurated but not ulcerated A piece of linen suture about one inch long was found in one portion of this margin The openings in the stomach and the jejunum were then closed, as were those in the transverse mesocolon and the gastrocolic omentum A Horsley pyloroplasty was then performed Subtotal resection of the stomach was not performed because of the low acidity, the fact that the ulcer was well healed, and in addition because it was felt that the hernia had been the sole cause of the patient's symptoms

Postoperative Course—Convalescence was complicated by a mild bronchopneumonia, but throughout the stay in the hospital, following the operation, he had no abdominal symptoms On September 13, 1937, four weeks postoperative, a gastro-intestinal series showed a normally active stomach without retention or areas of tenderness or spasm (Figs 6 and 7) There was some deformity in the region of the pylorus due to the pyloroplasty

He was discharged from the hospital September 17, 1937, at which time he was entirely free from symptoms When last seen (nine and one-half months postoperative), he was still on a hyperacidity diet His weight had increased 25 pounds over what he weighed before the operation He had remained completely symptom-free The scar was firm and well healed

DISCUSSION—A case of hernia through the transverse mesocolon and the gastrocolic omentum is presented This hernia developed after a posterior short loop gastrojejunostomy had been performed at another hospital Apparently the edges of the opening in the transverse mesocolon had not been sutured either to the stomach or the jejunum at the time of the original operation A hernia of some of the loops of small intestine into the lesser sac is the expected outcome under these circumstances That the herniated intestine extended across the lesser sac and through a hole in the gastrocolic omentum would appear to be a rather unexpected complication Two possible explanations are suggested for this development (1) The lesser sac may have become so greatly distended with loops of small intestine that the rupture of the gastrocolic omentum was spontaneous, or (2) the opening may have been the result of the operative procedure It may have been opened accidentally and not sutured, or the type of gastrojejunostomy described by the Mayos, in 1905, in which the transverse mesocolon is opened, may have been performed without subsequent adequate closure about the distal end of the gastrojejunostomy

The symptoms and roentgenologic findings can be readily explained on the basis of the pathology found at the operation The relief from symptoms

with the patient in bed, which at the time was attributed to the diet and medication to a great degree, was actually due to the relieving of the pull against the edges of the holes in the gastrocolic omentum and the transverse mesocolon by the weight of the loops of small intestines and their contents. Each time the patient was put to bed, the pain disappeared, and each time he was permitted up, the pain recurred.

The filling defect, spasm and tenderness found in the first gastro-intestinal series (Fig 1) can be explained by the supposition that a loop of small intestine was partially wrapped around the gastrojejunostomy. The later pictures showing the dilated loops of small intestine and these loops lying high up against the greater curvature of the stomach presented exactly the condition found upon opening the abdomen. Had the condition which was found at operation been considered preoperatively, the story of recurrence of pain each time the patient resumed the erect position for any length of time, taken together with the roentgenologic findings, should have made a correct diagnosis possible. Simultaneous clysis and gastro-intestinal series, with the films taken laterally or obliquely, would have probably shown the condition very plainly, particularly so if stereoscopic films had been made.

This case report bears out the statement that is so often made in the description of the technic of posterior gastrojejunostomy, that the edges of the opening in the transverse mesocolon must be closed about the stomach or the gastrojejunostomy suture line in order to avoid herniation into the lesser peritoneal sac. That this condition is not seen frequently is undoubtedly due to the fact that this step in the operation of posterior gastrojejunostomy is practically always carried out.

REFERENCE

- ¹ Moynihan. Duodenal Ulcer, 1912

MELANOSIS COLI

AN ATTEMPT AT ITS EXPERIMENTAL PRODUCTION
BY REPEATED ADMINISTRATION OF CASCARA SAGRADA

WARREN C. CORWIN, M.D.

FELLOW IN EXPERIMENTAL SURGERY, THE MAYO FOUNDATION

ROCHESTER, MINN.

BARTLE¹ apparently was the first to refer to a possible relationship between the cascara habit and melanosis coli. Bockus, Willard and Bank,² in 1933, reviewed the opinions of the various authors on the anthracene purgatives, all of which are said to act largely on the colon and stated that in every one of their cases of melanosis, in which a history of taking laxatives could be obtained, cascara or some other member of that family of laxatives had been taken daily for long periods just previous to the finding of the colonic

pigmentation They concluded that "the anthracene laxatives either contain a pigment or elaborate one within the colon which is phagocytized by the deep mucosal cells causing melanosis " In 1935, Zobel and Susnow⁶ observed melanosis coli in seven of 200 consecutive persons who underwent sigmoidoscopic examinations, and reported that the chief, apparent, causative factors were chronic constipation and the use of anthracene laxatives over a long period Quite the same view is held by Buie,³ who, in 1937, reported on a group of 571 patients who had melanotic deposits in the colonic mucous membrane "When it is considered," he stated, "that practically all patients who have melanosis coli are constipated, the likelihood that colonic stasis and its effect on the metabolism of foods may play significant rôles in the production of this condition becomes impressive However, when it is recalled that more than 95 per cent of persons who are constipated, many of whom are not in the habit of taking cascara, show no signs of melanosis of the colon, one leans more to the belief that this drug, or one of its constituents, or one of its effects, is of significance as a causative factor "

Experimental Investigation—In order to study the effect of the ingestion of cascara on the development of pigmentation in the large bowel, three dogs, weighing approximately 15 Kg each, were given relatively large doses of this drug over a period of one year with a single period of rest of three weeks Each dog was given 15 cc of the fluidextract of cascara sagrada, before feeding, six days of each week On the seventh day the dog received neither the drug nor food The amount of cascara administered daily would correspond to a dose of two and one-half fluid ounces (75 cc) given to a man weighing 165 pounds (75 Kg) It was given in capsules of a capacity of 5 cc During the study the four following diets were employed for periods of approximately three months each

(1) A mixed diet, consisting of 35 per cent horse meat, 35 per cent cracker meal, 5 per cent bone ash, 10 per cent lard, and 15 per cent cooked tomatoes

(2) A high fat diet, consisting of 25 per cent horse meat, 25 per cent cracker meal, 5 per cent bone ash, 30 per cent lard, and 15 per cent cooked tomatoes

(3) A commercial canned dog food (Paid), with approximately 5 per cent of bone ash added

(4) A mixed diet consisting of dog biscuits, alternating with a mash made of ground horse meat, corn meal, oat meal, and bone ash

Because of the apparent relationship between constipation and melanosis coli, so frequently alluded to in the writings of clinicians, an effort was made to keep the dogs of this study more or less constipated It will be noted that in each instance bone ash was present in the diet The amounts stated above were nearly always sufficient to keep the stools well formed and at times even scybalous On two or three occasions diarrhea did appear but this was always easily brought under control by increasing temporarily the amount of bone ash in the diet

The condition of the mucosa of the large bowel was kept under surveillance by proctoscopic examination once every two weeks or so. Short ether anesthesia gave such excellent relaxation that it was always employed. Owing to the anatomy of the dog's colon, with its long mesentery, practically the entire colon could be visualized by means of an ordinary 24 cm. proctoscope. As is the case with human beings, repeated enemata of warm water before proctoscopy greatly facilitated the examination. A total of 19 proctoscopic examinations were made on each dog during the 12 months of the experiment. At no time were abnormalities detected. The mucosa in each instance retained its normal color and luster. At the end of the experimental period, two of the dogs were killed and postmortem examinations were made. There was no evidence of colonic pigmentation, either grossly or microscopically.

Discussion—Melanosis coli is a nondetrimental, pathologic disorder grossly recognizable in probably somewhat more than 1 per cent of all people.⁵ There is considerable diversity of opinion as to the exact nature of the pigment involved. Recent writers on the subject are inclined to believe that the etiology of the condition is in some way connected with chronic constipation and the cascara habit. The investigations reported in this paper were carried out on dogs, and it must be borne in mind that the differences in anatomic arrangement and relative length of the colon of man and of the colon of the dog may be associated with physiologic differences. It may be concluded, from these investigations that in dogs which are prevented from having diarrhea by feeding bone ash, ingestion of large amounts of cascara over a long period of time is not sufficient in itself to produce pigmentation of the mucosa of the colon. This would indicate that other factors are at work in the genesis of this lesion. It may be, as has been suggested by Huist,⁴ that the chief factor in the etiology of melanosis coli is the artificial diarrhea produced by aperients taken on account of constipation or the fear of constipation. According to this idea, the aromatic protein disintegration products resulting from the diarrhea are absorbed by the mucous membrane of the colon and are there converted into pigment. In an attempt to affirm this statement experimentally, diarrhea artificially produced by means of daily catharsis should be maintained in dogs over long periods of time.

SUMMARY

Three dogs, each of which received 15 cc. of fluidextract of cascara sagrada 294 days in one year, failed to show any evidence of melanosis coli.

REFERENCES

- ¹ Bartle, H. J. The Sigmoid, Anatomy, Physiology, Examination and Pathology. *Med Jour and Rec*, 127, 521-524, May 16, 1928.
- ² Bockus, H. L., Willard, J. H., and Bank, Joseph. Melanosis Coli, the Etiologic Significance of the Anthracene Laxatives. A Report of Forty-one Cases. *JAMA*, 101, 1-6, July 1, 1933.
- ³ Buie, L. A. *Practical Proctology*. Philadelphia, W. B. Saunders Company, 419-425, 1937.

- ⁴Hurst, Arthur Melanosis Coli, with a Description of Two Cases in Which it Disappeared Whilst under Observation Guy's Hosp Rep, 87, 332-342, 1937
- ⁵Lockhart-Mummery, J P Quoted by Buie, L A¹
- ⁶Zobel, A I, and Susnow, D A Melanosis Coli Its Clinical Significance Arch Surg, 30, 974-979, June, 1935

EVISCERATION CAUSING RUPTURE OF JEJUNUM

CASE REPORT

JOHN R ORNDORFF, M D, AND HARRY E MOCK, M D

CHICAGO, ILL

FROM THE 'C' SURGICAL SERVICE OF ST LUKE'S HOSPITAL CHICAGO, ILL

ABDOMINAL wound dehiscence occurs in approximately 1 to 2 per cent of cases Glenn¹ has reported an incidence of 0.67 per cent wound dehiscence in cases operated upon where the pathology was nonmalignant, and 1.20 per cent where malignancy was present Dehiscence may be of varying degree, from simple peritoneal separation to the extreme of complete disruption with evisceration

Rupture of small intestine is a frequent accident It is often complete, and occurs following various traumata, with or without penetration of the skin However, an instance of dehiscence and evisceration causing complete rupture of intestine is a rare coincident

Muscular effort can result in rupture of intestine Wilensky and Kaufman² have collected 43 cases where rupture of intestine followed strenuous muscular effort In at least 33 of these a hernia was present, which they believe acted as a predisposing factor, perhaps furnishing a recess into which the antimesenteric border was forced and ruptured Mage³ recently reported an instance of severe muscular exertion, 102 days postoperatively, causing a 2.5x5 cm rupture in the wall of a segment of ileum adherent in the scar of a cholecystectomy wound

Case Report—E T, white, male, age 58, was admitted to St Luke's Hospital, Chicago, June 9, 1937, with a history of 30 pounds weight loss, and symptoms suggesting a carcinoma of the colon Barium clysmas showed partial obstruction at the splenic flexure The Wassermann test was negative After a prophylactic blood transfusion, a preliminary cecostomy was constructed Twelve days later the abdomen was explored through a left midrectus incision A carcinoma was found at the splenic flexure It was moderately fixed, but operable However, the liver was found studded with innumerable hard, apparently metastatic nodules The incision was closed in anatomic layers, using plain and chromic catgut without a drain The bowel had not been penetrated, and no biopsy had been taken

Postoperative Course—Convalescence was uneventful except for a small stitch abscess in the middle of the wound which suppurated a very small amount until the eleventh day The cecostomy functioned satisfactorily A many tailed bandage was in place constantly

RUPTURE OF JEJUNUM

On the thirteenth postoperative day the sutures were removed. The next morning, the fourteenth postoperative day, 12 hours after removal of sutures, the patient turned on his side. He related that a slight breeze seemed to chill the perspiration on the back of his neck. Immediately he was aware of the onset of a desire to sneeze. Although he protected his wound region with both hands, as he sneezed he felt it give way, beginning at the upper end. He experienced no pain. He stated that he believed the separation involved only the upper three-fourths of the wound.

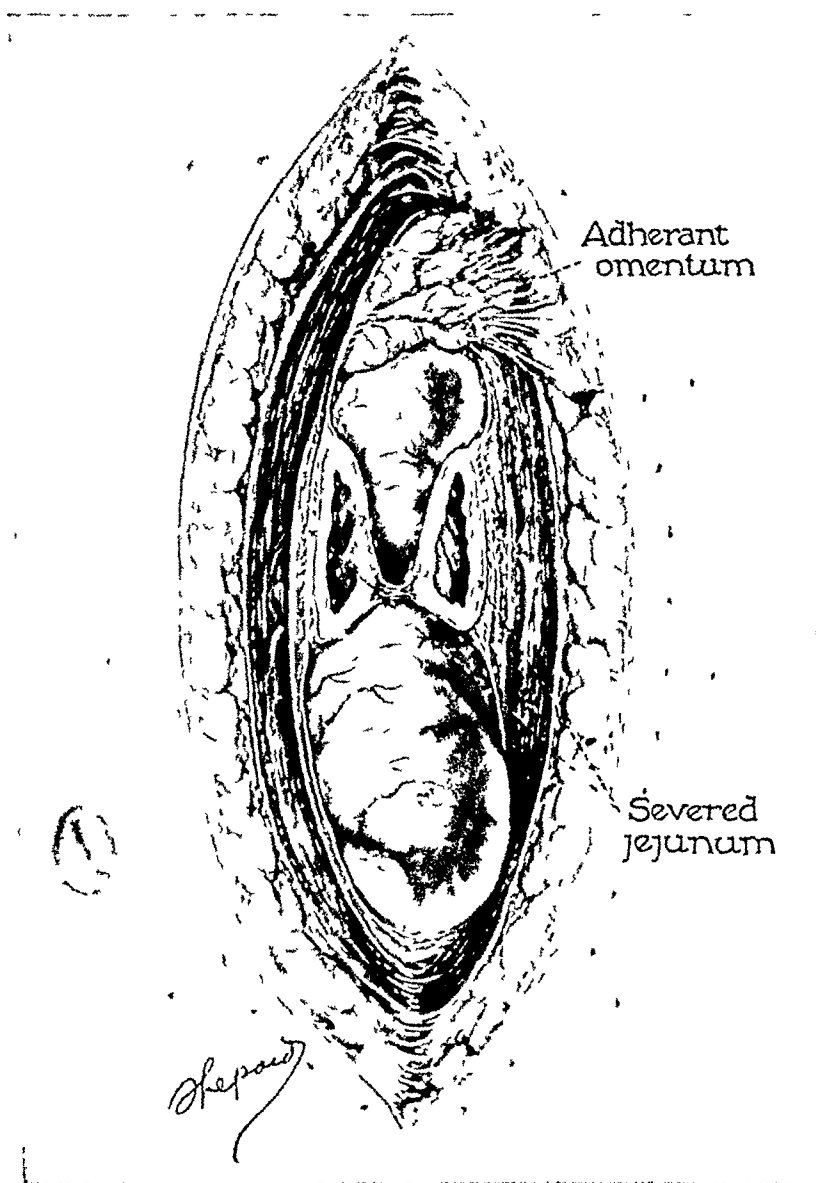


FIG 1—Appearance of wound one and one half hours after complete evisceration. The intestine has been replaced and wound separation completed in lower angle for better exposure. The ruptured jejunum may be seen in the middle of the wound, and adherent omentum in the upper angle.

Operation—The cecostomy tube was found intact. On removing the dressings, approximately 70 cm of small intestine was found lying on the skin of the abdominal wall, and the separation was over the upper three-fourths of the wound's length, as the patient had thought. When the coils of intestine were replaced the ruptured jejunum was visible (Fig 1). At the middle of the wound, on opposite sides, about the level of the umbilicus, two open stomata of small intestine were seen. Each was firmly adherent to the parietal peritoneum and directly faced each other. Leading from each stoma a segment of intestine extended laterally, and for about 10 cm was very firmly adherent to the ventral

parietal peritoneum The plane of each stoma was exactly at the border of the wound margin, and perpendicular to the lumen, the edges were smooth, as if made by scalpel The loop was determined to be jejunum Omentum was moderately firmly adherent in the upper third of the wound to the level of the subcutaneous tissue The carcinoma of the splenic flexure had increased in size since the exploration

The jejunum was mobilized sufficiently to permit construction of an end-to-end anastomosis The wound was again closed in anatomic layers using plain and chromic catgut, braided silk retention sutures, and black silk in the skin No drains were placed

Convalescence following the secondary closure was uneventful, and the patient was discharged with the wound firmly healed, though by second intention in its middle third

COMMENT—Evidently, an unusual mechanical accident had occurred The loop of jejunum had become so firmly adherent, transversely, to the ventral parietal peritoneum under the wound that on the instant of wound separation it ruptured, tearing cleanly across, as if incised

An early partial dehiscence had apparently occurred, as the omentum was moderately firmly adherent to the subcutaneous tissue in the upper third of the wound The peritoneum had separated earlier, and the omentum for some time had been lying superficially

The subcutaneous position of the omentum recalls the belief of Freeman⁴ that in many instances the primary cause of dehiscence is a closure of the peritoneum, through gaps in which omentum forces itself, and in swelling acts as an expanding wedge that forces the tissues apart, preventing proper union

REFERENCES

- ¹ Glenn, F, and Moore, S W Disruption of Wounds Surg, Gynec and Obstet, 65, 16, July, 1937
- ² Wilensky, A O, and Kaufman, P A Subparietal Rupture of the Intestine Due to Muscular Effort ANNALS OF SURGERY, 106, 373, September, 1937
- ³ Mage, S Rupture of Intestine into Abdominal Scar ANNALS OF SURGERY, 107, 472, March, 1938
- ⁴ Freeman, L Cause of Postoperative Rupture of Abdominal Incisions Arch Surg, 14, 600, 1927

PARATYPHOID FEVER COMPLICATED BY RUPTURED APPENDICITIS

STUART ZEH HAWKES, M D, M Sc D

NEWARK, N J

TYPHOID and paratyphoid fevers are known to attack the lymphoid tissue (Peyer's patches) of the small intestine, often causing perforation by ulceration Such a complication is not infrequent in either of these fevers, although it is more common with typhoid fever In the appendix these same lymphoid accumulations are present, being more pronounced in children and young adults, usually becoming more atrophic as the individual becomes

older Although this is the case, appendiceal perforation associated with these fevers occurs much less frequently than it does in the ileum Oslei,¹ in speaking of perforation, quotes McKenzie's collection of 265 cases in which the appendix was perforated nine times It seems strange that it does not occur more often

Boyd² states that in typhoid fever the lymphoid tissue of the appendix may show the infiltration with endothelial cells which is such a characteristic change in the ileum Cope,³ in discussing the differential diagnosis between appendicitis and typhoid fever, believes that typhoid fever is occasionally mistaken for appendicitis because of the abdominal pain and tenderness which are sometimes localized in the right iliac fossa He also states that a true typhoid appendicitis is sometimes seen, and cites a case upon which he operated and in which the symptoms of a true typhoid appendicitis initiated the illness MacCallum⁴ states that a similar process of ulceration as is seen in the Peyer's patches of the ileum takes place in the colon and also in the vermiform appendix, and that it is not uncommon to have a perforation in the base of an ulcer in the latter situation Sloan⁵ states that true acute appendicitis is a recognized complication in typhoid fever aside from the incidental involvement of the lymphoid tissue of the appendix early in the disease The appendicular pain associated with the swelling and ulceration of the lymphoid tissue in the appendix during the early stages of typhoid is not infrequently diagnosed as appendicitis

It would seem, then, that in association with typhoid or paratyphoid fever, there occurs an involvement of the lymphoid tissue of the appendix as well as the lymphoid tissue of the small bowel The right lower quadrant pain which is mentioned in the classic description of the disease may then be signs directly referable to pathologic changes occurring in the appendix If the pathology is marked, the process in the appendix may cause acute inflammation or perforation, just as it occurs with other organisms

Although it has been shown that the appendix is apparently quite often involved in the disease process, as well as other parts of the small intestine, a study of the literature reveals very few case reports of acute appendicitis complicating the disease Vidal,⁶ in 1913, cited such a case occurring on the sixth day of the general infection in a girl, age 13 The infecting organism was a paratyphoid B He states that a paratyphoid infection is not a contraindication to intervention Paisons,⁷ in 1927, made a careful study of the literature in reporting a case of typhoid fever complicated by a perforated appendix in a male, age 25 In this case there was also a perforation of the ileum The patient recovered In his study of the literature he collected 30 cases due to typhoid fever, the first case being reported by Sands in 1857 He believed that when definite appendicitis occurs in typhoid fever the mortality will be lowered by removing the appendix It is interesting to note that until about 10 years ago, all the cases reported complicated infections with the typhoid bacillus except the one case reported by Vidal However, in reviewing the literature for the past 10

years, all the cases reported, except five, associate the acute appendicitis with the paratyphoid organism

Wilde⁸ reported a case in 1930, similar to the case reported here, in which a diagnosis of acute appendicitis was made and the operation performed before complicating paratyphoid fever was recognized. The operation was followed by a febrile reaction on the third day, which proved to be of paratyphoid origin. Bernstein,⁹ in the same year, reported a girl, age 14, who was admitted with typhoid fever. She developed signs of acute appendicitis on the thirteenth day of the disease. A perforated gangrenous appendix was removed 11 days later, after conservative treatment was employed. A culture of the pus from the peritoneal cavity was negative for typhoid organisms. Rosenthal¹⁰ reported, also in 1930, the case of a child, age 14, who had been ill for two days with symptoms of appendiceal colic. At operation, the appendix was found to be acutely inflamed. A number of swollen patches in the small intestine were found and they suspected a possible typhoid infection. The organism isolated was a paratyphoid B. In 1931, Rose¹¹ reported the case of a girl, age 12, with acute appendicitis who was operated upon and who was later proven to be suffering from paratyphoid B fever as well. The symptoms of appendicitis occurred on the third day of her illness. Muller¹² in 1933, reported a case of a girl, age 16, who had nausea, vomiting and severe diarrhea. She was observed for three days and then operated upon because of signs of acute appendicitis. At operation, a perforated appendix was found. She had a positive stool culture for paratyphoid "Breslau." He makes the statement that it was a good thing for the patient that the stool culture was not known until after the operation or it might not have been performed, indicating that they might have attributed all the symptoms to paratyphoid fever.

In 1934, Mayer¹³ summarized the foreign literature on "paratyphoid appendicitis." He believed that the organism was often harbored in the appendix, in the same manner as the typhoid organism is harbored in the gall-bladder. He subdivided the cases into three classes: (1) Those in which there was a local disease of the appendix with no other gastro-intestinal lesions or generalized illness, (2) those in which the appendiceal signs occurred at the beginning of an illness and initiated the first signs of a paratyphoid infection, (3) those in which the general symptoms occurred first and somewhere in the course of the disease the patient began to complain of pain localizing in the right lower quadrant. He collected cases from the literature to illustrate these three different groups. He also states that the paratyphoid organism is often found in the gastro-intestinal tract of normal people in good health. He quotes Woltson who made a careful study of 28 appendices, in five of which paratyphoid organisms were found in the wall of the appendix, although the urine, blood, and stool of the patient were free of organisms. This paper gives an excellent review of the different opinions on the subject and summarizes many of the cases reported in the foreign literature.

Ramm¹⁴ summarized 349 autopsies of cases dying of typhoid fever. Three of these had perforated appendices. In his own experience he had operated upon four suspected cases, but involvement of the appendix was found in only one of these. In this case cultures showed both a typhoid and paratyphoid organism.

In 1937, Massabuau¹⁵ cited three cases which he had observed, one, in a female, age 34, who had great distention of the abdomen with signs over McBurney's point. She was operated upon four days later and a subacute appendix was found with hyperplastic lymph follicles. The patient died. The second case was a girl, age 19, who had been sick for three or four days with severe diarrhea. Because of the extreme condition of the patient she was not operated upon, and died on the fourth day of the disease. The last case was that of a girl, age 22, who had been sick for three days with pain in the right lumbar region, nausea and vomiting. She had acute tenderness over McBurney's point, with tenderness in the right fornix upon vaginal examination. She was operated upon the day of admission. A subacute appendix was found. All these cases occurred in the course of severe typhoid fever.

Although a study of the mortality from typhoid fever in this county¹⁶ shows that by rigid health regulations and education the disease is being better controlled each year, we will still have to consider this complication. There seem to be no current statistics on paratyphoid fever, but presumably the ratio incidence follows that of typhoid fever. Nevertheless, because of the greater number of cases of appendicitis complicating paratyphoid fever reported in the past 10 years, it is a question whether the paratyphoid organism is less well controlled or whether the cultural differences were not classified in the earlier reported cases. Whatever the answer may be, it is certain that the complication of acute appendicitis must be borne in mind in the course of both these fevers, as some of the mortality is probably due to appendiceal involvement. In the case herewith reported, an infection by one of the typhoid group was not suspected until cultural studies were reported by the laboratory.

Case Report—E. W., male, age 23, was first seen April 27, 1938, complaining of headache and pain in the abdomen around the umbilicus, which had developed three or four hours earlier while at work. He had not vomited or felt nauseated. Previous history was entirely negative except for several attacks of sore throat during the past year and a tonsillectomy several months ago. He had not been out of the city limits for over a year. On examination, his temperature was 100° F, pulse 90, respiration 20. General examination was negative except for the abdomen. There was some tenderness in the left upper quadrant which was not marked. Otherwise the abdomen failed to show any localizing signs. Rectal examination was negative. The diagnosis of appendicitis was suspected but was not warranted in view of the lack of signs. He was advised to stay in bed and restrict his diet to liquids. During the night the pain became more severe and his abdomen became distended. He vomited once during the night. He had a severe headache and had several attacks of diarrhea. When seen the next day, about 24 hours after the start of his illness, he had very definite signs of acute inflammation in the right lower quadrant. The temperature was 102° F, pulse 124, respiration 26. There

was rigidity of the muscle wall, together with direct and rebound tenderness in the right lower quadrant. Immediate operation was advised. He was transferred to the Presbyterian Hospital, Newark, N. J.

Operation—The peritoneal cavity was opened through a McBurney incision, and disclosed a cloudy, milky, odorless fluid which did not seem typical of either a colon or Streptococcus infection. A culture was taken. The appendix was bulbous, covered with fibrin, wrapped in omentum, and showed a definite perforation at its base. It was removed and the stump inverted. Two Penrose drains were inserted through a stab wound, one being placed in the right coloparietal space, the other over the brim of the pelvis. The abdomen was closed in layers, three silk-worm gut tension sutures being inserted. The skin was approximated with clips after placing one rubber dam drain beneath the fascia. He left the operating room in good condition. He was given saline with glucose (5 per cent) solution intravenously every six hours. He was placed on his right side to promote drainage.

Postoperative Course—The abdomen became distended almost immediately after operation. He complained of nausea. Duodenal suction drainage through a Levin tube was started, but it did not relieve the distention satisfactorily. The next day the abdomen was somewhat softer but still markedly distended. There was no rigidity or localized tenderness. He had no vomiting and was passing flatus at intervals. His temperature continued to rise to 103.6° F. on the third day after operation, and then dropped to about the preoperative level. His condition seemed fair, although he was weak and listless with many complaints. Following a small transfusion on the third day after operation, his condition seemed improved. The wound was discharging thin, serous fluid. During the next two or three days his temperature dropped slightly to 100° F., although his abdomen remained very distended, and he complained of severe "gas pains." In spite of Levin tube drainage and low glycerine enemata, the distention seemed not at all controlled. Continued study was made to ascertain the causes of this distention and pain, and he was examined carefully for signs of some localizing process. No abscess could be found. A report of the smear of the fluid from the abdominal cavity had shown cocci in pairs and chains, and gram-negative rods. Cultures showed growth of nonhemolytic Streptococci and a gram-negative rod which was to be subcultured. The gram-negative rod on subculture was reported to be an organism belonging to the Salmonella (paratyphoid) group. It was then recognized that the appendicitis was part of a paratyphoid infection.

On the seventh day after operation, he was fairly comfortable, his pulse had dropped to 70, respiration was normal, and the temperature was ranging between 100.4° and 99.4° F. Many of his complaints were less severe and it seemed that he was improving gradually. The next day, however, he had an elevation of temperature with an aggravation of all his symptoms. The temperature reached 104° F. in the next 24 hours. The pulse rose to 134 and the respirations to 40. The abdominal distention again became acute. The next morning, the ninth day after operation, a rash was seen to be appearing over his body and by that night he was covered thickly with a macular eruption. The rash lasted for three days and as it disappeared his temperature and pulse rate subsided slowly again over the next five or six days. At this time the operative wound was discharging thick greenish pus. The rectal examination was negative. On the sixteenth day after operation he complained of pain in the right shoulder and the right upper quadrant of the abdomen. The distention increased again and the liver dulness was apparently higher than normal. A roentgenogram taken at this time showed the right diaphragm to be high and, again, a localized collection of pus was sought below the right diaphragm. His temperature rose to 103° F., pulse 120, and on successive days continued to "spike" each afternoon. On the twenty-eighth day he had a chill with a rise in temperature to 105.5° F. A needle was inserted in the right seventh intercostal space in the midaxillary line and introduced in several directions in an attempt to find pus. None was obtained. His abdominal distention was still acute, and it was

decided that because of the marked distention of the abdomen, the liver had been pushed high under the right diaphragm into an abnormal position, thus accounting for the roentgenologic findings and the high liver dulness. He was given another small transfusion and seemed to improve following it. He was not vomiting. He was taking a soft diet, with extra carbohydrate feedings, well. During the next two weeks his temperature gradually subsided. His abdominal distention remained. He was eating well and seemed to be gaining strength slowly. A stool culture on the thirty-third day after operation was positive for members of the paratyphoid B group. He was discharged from the hospital on the fifty-fourth day after operation, stool cultures having been found negative twice in the interim.

Further laboratory data showed the urine and stool both positive. His blood culture was negative. He had a positive Widal for paratyphoid B. White blood counts taken at intervals showed the highest count to be 11,400, 52 per cent polymorphonuclear leukocytes, and the lowest count to be 9,100, with 67 per cent polymorphonuclear leukocytes. Microscopic examination of the appendix showed the wall to be necrotic and infiltrated with hemorrhage and polymorphonuclear leukocytes. Pathologic diagnosis: Acute gangrenous appendicitis with perforation. The urine at the beginning of his illness showed a trace of albumen, good concentration, occasional leukocytes, no casts.

On leaving the hospital he weighed 115 pounds. During the past two months he has gained 22 pounds and at present weighs 10 pounds more than his previous highest weight.

A study of the stool of the members of his family for possible carriers was made, and it was found that his sister had a positive stool culture for a paratyphoid B organism. At the time she had the positive culture, she was completely free from symptoms and was working daily. She was isolated at home by the health authorities for six weeks, until two negative cultures were finally obtained. During this time she had no symptoms referable to the disease.

SUMMARY

There are several points to be drawn from this case as well as from those reported in the literature:

(1) The low white blood count with the low differential count might be misleading unless the possibility of an associated disease process is kept in mind.

(2) The involvement of the appendix may apparently occur at any time during the disease. When it occurs early at the beginning of the illness the picture is very confusing.

(3) The treatment indicated is the same as that in other types of appendicitis, *viz.*, operation. It is as much a surgical emergency as a small bowel perforation.

(4) The incidence seems to be more frequent in the past few years with paratyphoid B organisms than with others of the typhoid group.

(5) By bearing in mind the possibility of appendiceal involvement in the typhoid group, some of the mortality may be eliminated.

REFERENCES

- ¹ Osler, W. Principles and Practice of Medicine, p. 9. D. Appleton Co., New York, 1930.
- ² Boyd, W. Surgical Pathology, p. 314. W. B. Saunders Co., Philadelphia, 1933.
- ³ Cope, Z. Early Diagnosis of the Acute Abdomen, p. 73. Oxford Univ. Press, London, 1927.

- ⁴ MacCallum, W G Text-Book of Pathology, p 603 W B Saunders Co, Philadelphia, 1926
- ⁵ Sloan, H G Lewis' Practice of Surgery, 7, Chap 3, p 4 W F Prior Co, Hagerstown, 1929
- ⁶ Vidal, F Bull de l'Acad de Med Paris, 69, 283-286, 1913
- ⁷ Parsons, W H New Orleans Med and Surg Jour, 79, 893-896, 1927
- ⁸ Wilde, J F Brit Med Jour, 16, 1930
- ⁹ Bernstein, M Ann Int Med, 3, 8, 1930
- ¹⁰ Rosenthal, M Zentralbl f Chir, 57, 1597-1598, 1930
- ¹¹ Rose, S A Arch Pediat, 48, 785-790, 1931
- ¹² Muller, H Munchen med Wchnschr, 80, 1688-1689, 1933
- ¹³ Mayer, J B Mitt a d Grenzgeb d Med u Chir, 43, 550-556, 1934
- ¹⁴ Ramm, M Sovet Khir, 6, 701-703, 1934
- ¹⁵ Massabuau, *et al* Arch Soc d sc med et Biol de Montpellier, 18, 233-240, 1937
- ¹⁶ Typhoid in the Large Cities of the U S in 1937 (26th annl rept) J A M A, 111, 414-418, 1938

ADENOCARCINOMA OF THE TRANSVERSE COLON IN A BOY AGE FIFTEEN *

OPERATION AND RESULT

CONSTANTINE J MacGUIRE, JR, M D

New York, N Y

Case Report—Hosp No 2523-38 G P, white male, age 15, was admitted to the First Medical Division of Bellevue Hospital June 16, 1938, after having been treated in the Medical Clinic. He gave a history of pain in the upper abdomen upon making certain movements of the torso. Onset about five weeks before admission. He was not nauseated, had not vomited and had had no other difficulty. The pain was dull and felt like a muscle cramp, it was transient in character. He had no diarrhea or constipation, no jaundice, no tarry, clay colored or bloody stools. His bowels moved regularly night and morning. He had lost about 14 pounds in six months. Roentgenograms taken in the Out-Patient Department were interpreted as indicating carcinoma of the transverse colon.

Physical Examination—There was a hard, movable, nontender mass, about the size of an egg, just above and to the left of the umbilicus. The rest of the examination was essentially negative.

Operation—July 5, 1938 (C J MacGuire). A very hard mass was disclosed arising from the middle portion of the transverse colon, as large as a man's fist. It was annular and partially obstructed the colon. It extended to, and involved the greater curvature of the stomach, and a fistula had formed between the process in the colon and the process in the stomach. There were many enlarged, edematous and moderately hard lymph nodes in the greater and lesser omenta and extending back to the roots of the mesentery. The foramen of Winslow was closed by adhesions.

In view of the involvement of the stomach and colon, the gastrocolic fistula and the imminence of more complete obstruction in the colon, resection *en masse* of the stomach and colon was decided upon, in spite of the fact that the widespread lymph node involvement indicated very little chance of permanent cure.

* Presented before the New York Surgical Society, November 9, 1938. Submitted for publication December 28, 1938.



FIG 1—Appearance of the gastrocolic fistula from the colonic side

Accordingly, the distal two-thirds of the stomach and most of the transverse colon were excised, and the jejunum anastomosed to the open end of the stomach. The

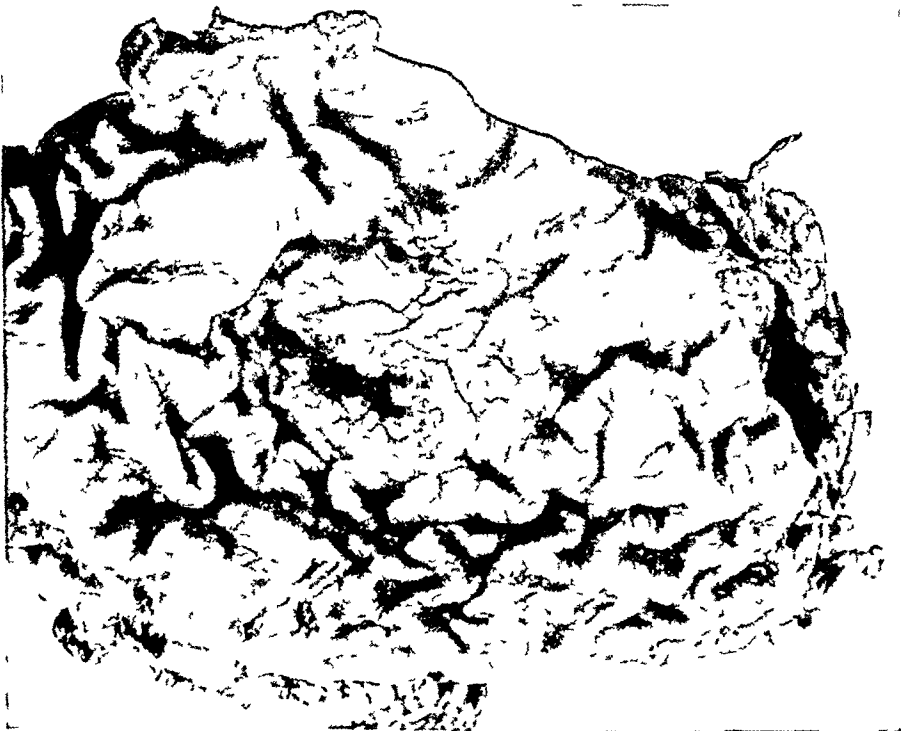


FIG 2—Appearance of the gastrocolic fistula from the stomach side

hepatic and splenic stumps of the colon were closed and the sigmoid brought over and anastomosed to the first portion of the ascending colon side-to-side. The abdominal wound was closed without drainage.

Pathologic Examination—Doctor Bevans The growth was a typical adenocarcinoma of the colon, with direct extension to and with involvement of the stomach The cells were growing in wild profusion with very little uniformity The lymph nodes showed only a mild hyperplasia, and showed nothing suggesting malignant metastases

After a couple of stormy days the patient made a smooth convalescence, and left the hospital on the nineteenth day postoperative, the wound having healed by primary union

The case is presented mainly because of the age incidence Carcinoma of the transverse colon is quite rare at the age of 15 It is shown also because of the satisfactory functioning of a side-to-side anastomosis between the sigmoid and the ascending colon I do not think that the blind loops, either hepatic or splenic, will cause trouble as they drain by gravity and may be of some advantage in fluid absorption as there has been no diarrhea at any time since operation The patient has gained 27 pounds The prognosis is, of course, very uncertain

PRIMARY CARCINOMA OF THE COMMON BILE DUCT *

RESECTION END-TO-END ANASTOMOSIS

JOHN H GARLOCK, M D

NEW YORK, N Y

FROM THE SURGICAL SERVICE MT SINAI HOSPITAL N Y

Case Report—Hosp No 421221 H H, female, age 53, was admitted to the Medical Service of the Mt Sinai Hospital, March 10, 1938, with the history of three weeks previously, without any preceding symptoms, having vomited several times and having noted, the following day, itching of the skin, darkening of the urine, light colored defecations, and an increasing jaundice One week after the onset, she experienced an attack of severe, cramp-like epigastric pain coming on after lunch, which lasted five hours There has been no pain since then She had never had a similar episode She had lost five pounds in weight Past and personal histories were negative

Physical Examination showed an active, alert, middle-aged woman who was deeply jaundiced Heart, lungs and abdomen negative There was no palpable enlargement of either the liver or gallbladder The spleen was not palpable Blood pressure 126/80

Laboratory Data—Hemoglobin 99 per cent, white blood cells 6,700, polymorphonuclear leukocytes 44 per cent, lymphocytes 43 per cent, monocytes 9, and eosinophiles 4 Stool examination Brown, guaiac negative, urobilin trace Galactose tolerance test, which was repeated three times, showed an excretion of 5 Gm Urinalysis Specific gravity 1022, negative for sugar and albumen Bile 3+ Urobilin $\frac{1}{2}$ to $\frac{1}{10}$ No tyrosine Urea nitrogen 8, blood sugar 80, cholesterol 290, cholesterol ester 87, icteric index 21, bilirubin 3.0 Wassermann negative, van den Bergh direct, positive Takata-Ara 4+ Total proteins 7.0 The sodium d-lactate test indicated liver damage

It was the consensus of opinion that the constant urobilin in the stool, the absence of hypercholesteremia, and the liver function tests all pointed toward hepatitis as the cause of the jaundice rather than an obstruction However, at the insistence of the

* Presented at the New York Surgical Society, November 23, 1938 Submitted for publication January 5, 1939

CARCINOMA OF CHOLEDOCHUS

attending physicians, operation was undertaken. This was performed March 24, 1938, after two preliminary transfusions of 500 cc of citiated blood.

Operation—Doctor Garlock. Under ethylene-ether anesthesia, an upper right rectus incision disclosed the liver enlarged to about three fingers' breadth below the costal margin. Its anterior edge was rounded. The viscus appeared normal except for a slightly greenish color and a faintly mottled nutmeg appearance. Duodenum and stomach were normal. The gallbladder was of normal consistency and partially collapsed. Palpation revealed a thickening in the region of the common bile duct at its junction with the cystic duct. It was the operator's first impression that this represented an enlarged lymph node, but it was thought advisable to demonstrate the gross

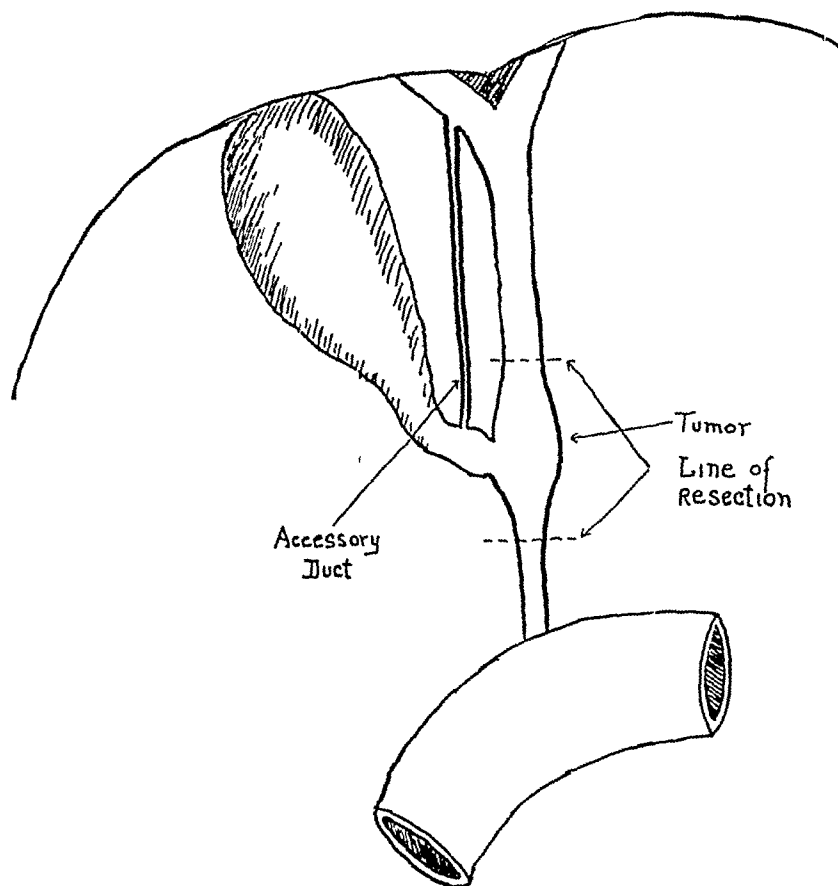


FIG 1—Diagrammatic sketch of the findings at operation. The accessory cystic duct is indicated. This was ligated and divided.

pathology more definitely. Accordingly, it was found necessary to dissect out the common duct in this situation. There was disclosed what appeared to be a primary neoplasm involving the common duct at the point of junction with the cystic duct. There were no enlarged lymph nodes either visible or palpable. Because the growth seemed to involve the cystic duct, utilization of the gallbladder for anastomotic purposes was out of the question. A radical procedure was decided upon, namely, excision of a segment of the common duct containing the tumor together with the cystic duct and the gallbladder in a block dissection (Fig 1).

Operative Procedure—The common duct was dissected away from the portal vein as far as the hilus of the liver. Above the tumor, the duct was found to be considerably dilated and thickened. Below the growth, it was collapsed and thin-walled. During the dissection, an accessory cystic duct was demonstrated. It apparently communicated with the right hepatic duct and was inserted into the upper aspect of the cystic duct below (Fig 1). This accessory duct was minute and barely admitted the end of a fine

probe. The gallbladder was dissected from its bed, the cystic vessels ligated and divided, and the common duct cut across above and below the tumor, with a wide margin of normal duct on each side of the tumor (Fig 2). The accessory cystic duct was ligated, after an unsuccessful attempt to intubate it for purposes of external drainage. The entire specimen was removed in one piece. The remaining segments of the common duct were mobilized, and it was found that they could be brought together with very little tension. A T-tube was inserted and the divided duct repaired with interrupted sutures of fine silk. Two cigarette drains were placed down to Morrison's space and the wound was closed in layers.



FIG 2.—Primary Carcinoma of the Common Bile Duct. The tumor is indicated by 'x' and extends into the cystic duct. The gallbladder did not contain calculi.

Subsequent Course—Convalescence following this procedure was uneventful except for a rise in temperature of unexplained origin, to 104° F, occurring on the eighteenth day. The icterus index dropped to 2, and the stools became brown. The T-tube was left in place and the patient was discharged on the thirty-eighth postoperative day (Fig 3).

Pathologic Examination—Dr Paul Klemperer, Path No 62336. The specimen showed the presence of an adenocarcinoma of the common bile duct, which also involved the cystic duct at its entrance into the common duct (Fig 4).

Follow-Up—The T-tube was removed June 2, 1938 approximately two and one-half months after the operation. The sinus tract healed in a few days. The patient has remained well since. There has been no pain, jaundice, or temperature rise. Bowels are moving normally, and are of normal color and consistency. There has been a gain of 25 pounds.

This patient is presented for a number of reasons. First, too great reliance should not be placed upon laboratory tests in differentiating obstructive jaundice from jaundice of hepatogenous origin. In this patient most of the laboratory tests indicated that the jaundice was probably due to liver damage rather than obstruction. Second, primary carcinoma of the common bile duct is a rare condition, and, more rarely, cannot be handled by radical surgery at the time the patients present themselves for treatment. Third, to call attention to the fact that wide sections of the common duct may be removed and end-to-end suture performed if adequate mobilization of the remaining portions of the duct is carried out. Fourth, to emphasize the fact that initial repair of common duct injuries does not as a rule produce strictures such as are encountered following late secondary repairs.

DISCUSSION—DR SEWARD ERDMAN (New York) said, with regard to the immediate repair by end-to-end suture, that he recalled a case he had presented before the New York Surgical Society, in 1932, at a period of about five months after repair of a resected duct. Accidentally, at the first operation, 25 cm of the common duct was excised, but was immediately

repaired by end-to-end suture over a T-tube. The patient last reported at the Follow-up Clinic in June, 1937, stating that he had had recurrent attacks of colangitis throughout the five years, the first beginning five months after operation. For two years they were rather frequent, but had



FIG. 3—Cholangiogram following the injection lipiodol through the T tube, demonstrating the continuity of the common duct and its patency into the duodenum

become less so. Dr. Ellsworth Eliot, in 1936, assembled a total of approximately 180 cases in an article on the late results of injuries to the common duct and its attendant repair, and classified them according to the type of operation undertaken. The paper was read at a meeting and dis-

cussed by Walters, of The Mayo Clinic, who in discussing the paper, stated that, up to then, he had had more than 40 cases. Lahey, also, stated that he had seen more than 20 cases, which increased the total to 240. Despite numerous operations that have been devised, many of which are very ingenious, the best results—and this is a qualified “best”—are obtained when it is possible to effect an end-to-end suture. The attempts to bridge over a duct defect with a T-shaped rubber tube or by a rubber tube left in the duct, and even the hepatoduodenostomies show only a few successful cases that have lived 10 to 15 years. Lahey stated that he had performed 14 im-

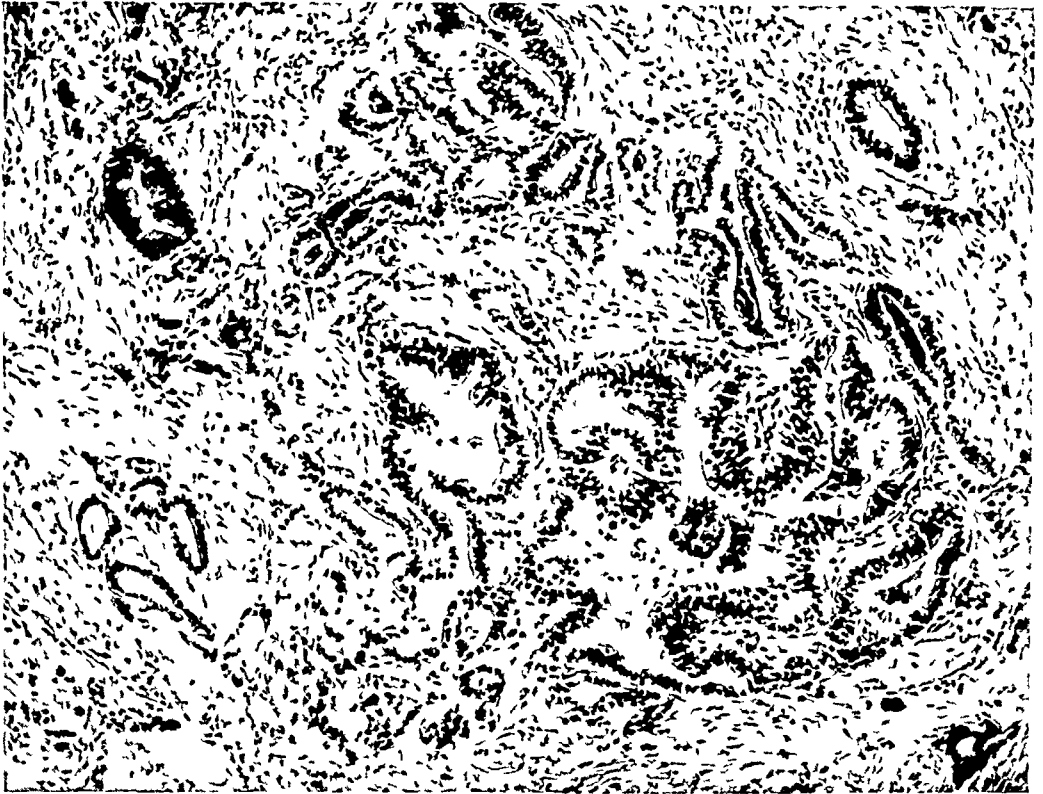


FIG 4—Carcinoma of the Common Bile Duct. Microscopic section showing the features of an adenocarcinoma.

plantations of the sinus into the stomach, using the external fistula tract, but that 12 were complete failures. In the present case presented by Doctor Garlock, the use of the end-to-end suture gives promise of a good result. The ordinary T-tube has the objection that when it is withdrawn, there is danger of kinking of the duct at that point or further tearing. McArthur has suggested the use of an L-shaped tube up the duct and the insertion of a small tube through the stem of the L which leaves the L through a hole at the angle and passes down into the duodenum. It is a movable tube, permitting irrigation and cleansing of the duct. In the case reported by Doctor Erdman, in 1932, the T-tube was left in so long that it became necessary to operate again to remove it. It had become blocked with calcium, causing an obstruction, in the sense that there was a complete external biliary fistula, and no bile could pass into the intestines through the blocked tube.

DR CARL EGGERS (New York) said that Doctor Garlock's case was interesting not only from the standpoint of presenting a removable primary carcinoma of the extrahepatic duct system, but also from the standpoint of technic employed, permitting a complete suture after resection of the specimen and mobilization of the common duct. Very few surgeons have a sufficient number of cases of this kind to draw conclusions from their own material, and have to be guided entirely by published results. In looking over the literature one finds that the lesion is encountered rather infrequently. Shapiro and Lifoendahl, in 1931, reported 15 cases of tumor of the extrahepatic bile ducts observed at Cook County Hospital, covering two and one-half years' study of autopsy material, of which three were benign and 12 malignant. Marshall, of The Mayo Clinic, wrote a paper on "Malignancy of the Extrahepatic System," in 1932, and stated that in a series of 22,000 operations upon the biliary tract during a 20-year period, 53 cases were encountered, four benign and 49 malignant. They were distributed in various portions of the ducts, including the papilla of Vater. All cases were proved by pathologic examination.

The treatment depends upon the location, as well as upon the extent of the growth. In the majority of the reported cases, either simple drainage of the duct above the obstruction was effected, or some form of anastomosis with the stomach or other portion of the intestine. Only rarely could a resection be performed. The cases suitable for radical extirpation have been carcinoma of the cystic duct or of the junction of the cystic with the common duct, or of the common duct itself. Carcinoma of the papilla of Vater has also been successfully removed. Doctor Garlock's case presented one of these favorably situated tumors, and it was small and limited to the duct. It emphasizes the importance of careful search in all cases of obstructive jaundice, for it is conceivable that it may have easily been overlooked. Doctor Garlock's resection of the gallbladder with the cystic duct and a portion of the common duct including the tumor and a safe portion of duct above and below it, has permitted him to present to us a very interesting and instructive specimen, one which it would be difficult to duplicate. He has, in addition to this, emphasized a point which perhaps none of us has sufficiently realized, that it is possible to mobilize the common duct to the degree that was accomplished in this case, and permit resection and later suture of the two ends. The radical procedure employed and the present excellent condition of the patient would seem to warrant a favorable prognosis.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M D
1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English

Exchanges and Books for Review should be sent to James T. Pilcher, M D, Managing Editor, 121 Gates Avenue, Brooklyn, N Y

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa

BOOK REVIEW

SURGICAL PATHOLOGY OF THE MOUTH AND JAWS By ARTHUR E. HEITZLER, M.D. Heitzler's Monographs on Surgical Pathology 1938 Philadelphia, Montreal and London J. B. Lippincott Co. 237 pages, with 206 illustrations Cloth

WITH the appearance of this volume by Doctor Heitzler, the author completes a series of ten monographs on surgical pathology. The preface recalls vividly the general tenor of his recent delightful, entertaining, and instructive autobiography, *The Horse and Buggy Doctor*.

The term monograph is peculiarly descriptive of Doctor Heitzler's writings, as it essentially describes the character of the contents of his publications, in that they are records of his personally observed cases. He does not refer to, or describe, cases or pathologic conditions which may have appeared in other treatises, with which he is not familiar. The references he quotes have, as he says, been collected for him by an efficient secretary, and he acknowledges that he has not read the original articles. Possibly this fact renders the present text all the more individual.

Clinical data and pathologic detail encountered by a surgeon, rather than another specialist, are well classified and have been expounded in a competent and most interesting fashion. In reflecting his clinical and operating room experiences in a field that not infrequently merges into another specialist's domain, the author, as usual, emphasizes the surgeon's self-reliability as compared with laboratory pathology. There is no mention of tumor grading for prognosis, although there is recourse to frozen section and usage of biopsy material. The detailed observations and assembled facts, together with mature and critical comment, well establish the worth of the volume.

The chapters include lesions found originating from the lips, mouth and tongue, gums, palate, nasopharynx, larynx, and of dentigerous origin. Brevity in certain subjects is occasioned by a practical attitude surgically and, possibly, by a paucity of first-hand case material. The text is embellished with numerous illustrations, gross and microscopic, and all excellent. Many of the gross are notable, as pathologic states of the mouth do not lend themselves well to photography.

Whether agreeing with all conclusions or complaining of brevity of subject, the reader will find both the clinical and pathologic data authentic and useful in a field that to-day is being regarded as less of the surgeon's and more of the rhinolaryngologist's or dentist's. The book is highly recommended to those specialists, the pathologist, and particularly to the general surgeon.

IRVING M. DERBY

CORRECTION

In the article by Brown, James B. *The Utilization of the Temporal Muscle and Fascia in Facial Paralysis*. *ANNALS OF SURGERY*, 109, 1016-1023, June, 1939, the last word of the seventh line, page 1021, should be temporal, not masseter.

ANNALS OF SURGERY

VOL 110

OCTOBER, 1939

No 4



TRANSACTIONS OF THE AMERICAN SURGICAL ASSOCIATION

MEETING HELD IN HOT SPRINGS, VA

MAY 11, 12, 13, 1939

ADDRESS OF THE PRESIDENT

THE DEVELOPMENT OF NATIONAL SURGICAL SOCIETIES WITH THE ADVENT OF MODERN SURGERY*

DALLAS B PHEMISTER, M D

CHICAGO, ILL

MEMBERS of the American Surgical Association and Guests In opening the Scientific Session of this annual meeting I must first express my great appreciation of the honor of being chosen to serve as your presiding officer. During my 22 years of membership in this Association, I have attended all of the meetings except those of 1918 and 1926, at which times I was in Europe. The experiences which I have had during these years in listening to the presentations, in occasional appearances on the programs and in participating in the general fellowship of the Association are among the most treasured of my professional career.

For a topic of discussion I have chosen the development of national surgical societies with the advent of modern surgery. It is hoped that in addition to the general interest which other societies may have for us, their procedures may be found helpful in outlining the course of our own Association.

There was little need for special surgical societies of national scope until the advent of antiseptics since the advances in surgery up to that time were relatively slow and its practice was extensively concentrated in the large cities which were adequately served by local societies. Then, as progress almost overnight became exceedingly rapid, the demand arose for organizations to meet the needs of the profession of entire nations or of groups of

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

nations with a common language First came the establishment of general surgical societies, to which this discussion will be limited, and then followed the societies of the surgical specialties as those fields were developed

The oldest existing national surgical organizations are the Royal College of Surgeons of Scotland founded in 1505 and the Royal College of Surgeons of England founded in 1800 But they differ from surgical organizations which have followed outside the British Commonwealth in that their primary function has been to serve as examining and certifying boards They have never conducted annual surgical congresses for the discussion of scientific topics, their educational activities being confined almost entirely to lectureships In consequence, the Surgical Section of the British Medical Association, established in 1867, became the important British forum for the discussion of modern advances in Surgery It remains an active organization with an annual attendance ranging up to 400 members A special surgical society, The Association of Surgeons of Great Britain and Ireland, was founded as late as 1920, chiefly by the initiative of Lord Moynihan Its membership is limited to 250 surgeons, 200 of whom are active members and 50 associate members They meet annually for three days the first week in May in one of the university cities, every third meeting being in London Forenoons are devoted to papers and afternoons to operations and clinical demonstrations Its membership is drawn largely from the surgeons of the teaching hospitals and there is little discrimination between general surgeons and surgical specialists

The first modern society for the surgeons of a nation, or better stated, for the surgeons of any nationality using a common language, was the German Society for Surgery, established in 1872 Prior to that time the meeting place of German surgeons had been in the surgical section of the Society of German Natural Philosophers and Physicians It was eventually recognized as being inadequate for the needs of the growing specialty and at the annual meeting in 1871, Gustav Simon took the initiative for the organization of a separate society Consequently, on the invitation of Simon, Langenbeck and Volckmann, a meeting was called for the following April and the German Society for Surgery was formed It has always met annually in Berlin for three and one-half days during the week following Easter There are four forenoon, one evening and three afternoon sessions and the annual dinner

The policy adopted for membership was very inclusive It was to be unlimited in number, anyone specializing in surgery, using the German language and recommended by two members of the society, was eligible for election subject to approval of the Executive Committee In consequence the membership grew rapidly from 81 for the first meeting to 651 in 1896, to 2,236 in 1914, and to 2,599 in 1933 After that it had declined to 2,264 in 1937, when the last statistics were published

In contrast to this inclusive policy for membership, an exclusive policy for administration and program was adopted and has been continued Langenbeck, the then recognized leader of German surgery, served as president

for the first 15 years, since which time the office has usually been occupied by one who has served for one year only. During the 68 years of its existence, only three men have served as secretary, to which office has been entrusted great responsibility in the selection of the programs. Guilt occupied the position for 28 years, Korte for 31 years, and Borchard has now served for nine years.

An endeavor is made to obtain for the program each year the most important advances in the entire field of surgery, which are presented to the society meeting as one body. There are usually 75 to 85 speakers. The presentations average ten minutes in length with the exception of certain special dissertations, which are longer. Discussions are numerous and criticisms free. The transactions were issued as separate publications, for the first 50 years, but have since appeared annually in one volume of the *Archiv für klinische Chirurgie*.

The influence of the German Society for Surgery on surgical progress has been enormous. In the first place, it has reached a great many persons. Because of its inclusive policy, its membership and the attendance at the congresses have been large, including many surgeons from states adjacent to Germany. Because of its lengthy programs and of the preference given to original work, irrespective of whether accomplished by one of the younger or older members, a remarkably high percentage of the advances which the German speaking peoples have made in surgery have first been presented at these annual congresses. This fact is obvious to anyone who examines the Transactions, which have been widely read, or who reads Friedrich Tiedelenburg's "The First Twenty-Five Years of the German Society for Surgery." At the same time, the scholarship of the presentations has been of an order that had served well to popularize the recent advances made elsewhere. It is safe to say that by pursuing the path advocated at the beginning, its large membership and extensive programs of high quality have led to much greater accomplishments on the part of its members and to much greater influence on German and world surgery than would have resulted from pursuing the path then advocated by Billroth, who preferred a small, intimate body which would issue no publications.

Surgery in France long centered to an unusual degree in Paris. The Royal Academy of Surgery, of glorious memory, existed from 1731 to 1793, when it, along with the other academies, was overthrown by the revolutionists with the famous explanation that "France no longer had need for men of learning." There was no further organization until 1843, when the Society of Surgery of Paris was formed. Its success from the first was great, but with the advent of the new era it is commendable that its own members took the initiative in the establishment of the French Surgical Association in 1884. The stated aims of the Association were "to advance the science of surgery and to establish scientific bonds between the savants and the practitioners of surgery." Membership was to be inclusive, and was made open to all French speaking surgeons regardless of nationality. It provided for a congress lasting six days which has been held annually in Paris.

during the first half of October. Two hundred fifteen members were elected at the first congress and the number increased rapidly so that for several years the membership has been in the vicinity of 1,200.

The sessions are held during the afternoons, the forenoons being principally devoted to attendance at clinics. At each of three sessions, the discussions are limited to two topics, usually related. An essayist is chosen for each topic one year in advance and his presentation is usually lengthy and scholarly. Then follow numerous short, prepared discussions, sometimes totaling 20 in number. At the other three sessions, miscellaneous papers are presented from the general field of surgery and its specialties. The congress has been an important implement for dissemination of surgical knowledge especially in France and the other Latin countries. A volume of transactions is published annually.

The Italian Surgical Society was formed in 1882, along lines somewhat similar to those of the German and French societies. Its annual meetings are held in Rome during the month of October. In 1937, its membership had grown to 721.

Surgical societies similar to those of Germany, France and Italy have been established in most of the other states of Europe and in South America and Japan. Since large inclusive medical societies like the American, Canadian and British Medical Associations, with their sections on surgery, do not exist in other countries, their large surgical congresses are of great national import for progress in surgery.

In the United States and Canada, a mixed course has been pursued as compared with Great Britain and continental Europe. A Section on Surgery of the American Medical Association has existed since 1860, and the attendance at the sessions in recent years has averaged more than 1,000 members. A surgical section has existed in the Canadian Medical Association since 1869, and recent attendances have reached as high as 300 members, when the meetings have been held in the large eastern cities. These sections have played an important part in the dissemination of knowledge to the general body of surgeons of the two countries.

Contrary to the situation in other parts of the world, two societies, the American Surgical Association and the American College of Surgeons, have come into existence to meet the special surgical needs of the United States and Canada. This resulted principally from the course that has been pursued by the American Surgical Association since soon after its establishment. The original plan, as reviewed so dramatically two years ago in the "dialogue" between President Evarts A. Graham and Founder Samuel D. Gross, appears to have been for a large society somewhat similar to those which have developed in Europe. Its membership was limited to 100 at the time of formation in 1880, and there were 91 fellows at the time of the first scientific meeting in 1882. But, the advisability of making it easy to enlarge the membership was immediately realized, as Doctor Gross stated in his opening presidential address, in 1883, that the Council was recommending an increase from 100 to 150 fellows to be voted at that meet-

ing The measure was apparently adopted but after the retirement of Doctor Gross the policy of expansion into a large society as surgery grew was not pursued and the limit for active membership remained as low as 150 until 1934 when, as a result of repeated appeals for enlargement, provision was made to increase it gradually over a period of five years to the present number of 175

As a result of this extremely conservative, almost inflexible, policy with reference to membership during a 51-year period of unprecedented growth in population, in surgery and in number of surgeons, the Association gradually became more and more exclusive. This left an ever increasing demand for a surgical organization to meet the needs of the large number of surgeons who were not being adequately cared for by the surgical sections of the American and Canadian Medical Associations

Franklin H. Martin, seeing this golden opportunity, started the Clinical Congress of Surgeons in 1910, and, in 1913, organized out of it the American College of Surgeons. It was started with 1,064 fellows and the number was rapidly increased until at the present time it amounts to 11,639, representing all fields of surgery, gynecology and obstetrics. In proportion to the number of physicians in the two countries, the membership from the United States is about twice as numerous as that from Canada. It serves both as a certifying body, by the granting of fellowships, and as an educational body through its annual five-day Clinical Congress, its sectional meetings and its publications. Both functions are definite drawing cards for membership and there is an average attendance at the annual Clinical Congress of about 3,000 fellows

Since the American College of Surgeons and the American Surgical Association are now both well established societies, they should be continued, each to serve the purposes for which it is best adapted. The American College of Surgeons, in addition to other functions, should aim at imparting knowledge through its congresses to a large body of the surgical profession, correcting its tendency to be too inclusive, so that it will not foster the performance of surgery by some who are inadequately qualified. On the other hand, the American Surgical Association, which is now destined to remain a relatively small organization, should only admit to fellowship those who are engaged more specifically in the advancement of the science and the art of surgery. Most men of this class are connected with medical schools, but all should be included who demonstrate their ability to make significant contributions to surgery whether by clinical or laboratory investigation, and whether they are connected with teaching or nonteaching institutions. With such a representation, it would be possible, at the annual meetings, to present the great majority of the advances made in surgery in the two countries to a group who, in turn, would make the greatest use of the information gained in practice, teaching and research. In other words, the Association should operate as a forum which fosters surgical education and research throughout the United States and Canada

It might be said that this has been the end for which the Association

has always striven. The Constitution states "The object of this Association shall be the cultivation and improvement of the science and art of surgery, the elevation of the medical profession and such other matters as may come legitimately within its sphere." But the Association does not function in these respects to the extent that it should in view of the significant name that it bears. The main reason for this is that the limited membership excludes too many of the ever increasing number of surgeons who are qualified to take part in the programs and who should profit by its proceedings. To repeat what has often been pointed out, the competition is so stiff that men are usually not elected to fellowship until they are mature surgeons unless they have accomplished outstanding investigations. The age limit is 30 years, but at present the youngest fellow is 38 years old and the average age of the active fellows is 53.9 years. That means that most of the presentations are of a sound and reliable nature, emanating from men of seasoned judgment and accomplished surgical technique. This type of work should always comprise a large part of the program. But most contributions that are notable for their fundamental originality, whether in the field of clinical or laboratory investigation, come from the younger surgeons, the majority of whom are now automatically excluded from fellowship. The present arrangement, whereby some of them appear on the program by invitation either as co-author or alone is helpful but is no real solution of the problem.

Also, the influence of the Association on the medical schools is not as widespread as it should be. There are 66 medical schools in the United States classified as acceptable by the American Medical Association, and nine medical schools in Canada. Of these, 27 in the United States and seven in Canada have no faculty member who is an active fellow of the Association. No plea is made for a wholesale admission of the teachers of these medical schools or of those schools which already have representation. However, a survey would undoubtedly disclose many suitable candidates in both groups.

The matter of sectionalism calls for discussion in this connection. The older, more prosperous and more densely populated sections are, in general, the seats of the better supported and more fully developed institutions, whose staffs have the greatest representation in this Association. But the newer and less densely populated districts must maintain institutions to serve their own needs and this they usually do as efficiently as their means permit. If the influence of the Association is to be disseminated as widely throughout the two countries as should be the case, somewhat greater allowance should be made for handicaps of these sections than is now made, and fellowship should be extended to more members of the staffs of their institutions than would be granted to those of similar accomplishments in more advantageous communities. The Association would then assist, more than at present, in elevating their standards. It is noteworthy that every medical school of any important European country has faculty representation in its national surgical association and that eligibility usually extends to those of the lower ranks.

Since the main purpose of the Association is the advancement of surgery, it should not shut itself off too much from the rest of the surgical world. If the advancement of the fellows themselves should ever become too prominent an aim, it might be accused, as was the Royal Society of Physicians and Surgeons of London just before its demise in 1905, of existing more for the exclusion than for the election of members.

Obviously, if more men are to be admitted from the ranks of the educators and investigators in surgery, the limit on membership in the Association will have to be appropriately increased and kept readily flexible. With the expressed goal of the Association kept firmly in mind, it would then be possible in the course of a few years to bring up the membership to a point of maximum efficiency. In order to adjust for the increased number of suitable papers that would be offered, a considerable proportion of them might be limited to ten minutes, as is the case with many special societies. In many cases all that is essentially new about presentations may be given before an audience of specialists in the field in ten minutes. With such an arrangement, even with the present freedom of discussion, it would be possible to present at least 45 papers during three full days instead of 32 as at the present meeting.

It is worth while for us to glance at what is being done correspondingly by our colleagues in the field of internal medicine. The youthful American Society for Clinical Investigation with 200 members, and the Association of American Physicians with 225 members, meet annually the first week in May at Atlantic City, the former for one day and the latter for the two following days. There is an extensive overlap in membership and in attendance of the two coordinated societies. Also, the meetings are open and in a large hall so that a great many nonmembers, mostly young and attached to departments of internal medicine, are welcome and privileged to be present. There are presented 25 to 30 ten-minute papers, principally of experimental work, by the Society for Clinical Investigation, and 45 to 50 fifteen-minute papers principally of clinical work by the Association of American Physicians. By this arrangement about twice as many papers are presented in the three days before three or four times as many persons as in the meetings of our Association.

The American Surgical Association has maintained a standard of integrity for membership which is one of its finest traditions. It is well expressed by the motto selected by Malgaigne for the Society of Surgery of Paris: "Truth in the science, morality in the art," and it should be safeguarded in any policy of future expansion. I want to conclude with my conviction that if provision were made for proper gradual enlargement of the membership, to comply with the available talent, the Association would enter a period of growth in which it would maintain its tradition for excellence of performance, stimulate more fellows to increased productivity, and steadily widen its much needed influence in the entire world of surgery.

REPAIR OF CRANIAL DEFECTS BY CRANIOPLASTY *

FRANCIS C GRANT, M D

AND

NATHAN C NORCROSS, M D

PHILADELPHIA, PA

✓THE EARLIEST INSTANCE of cranioplasty in man to which reference can be found is a case reported by J van Meekren, in 1670, in which a bone from a dog was used to successfully repair a cranial defect in a man. The graft was successful, but was removed because of the opposition of the Church to the use of an animal's bone in "marring God's image." ✓ This case was reported by Giekov, in 1901, and is quoted here from Pankratiev⁹⁹ (1933), the original literature not being available.

✓Over 200 years passed before any other reports of plastic operations performed upon the skull were published. During this interval much work on bone grafting in general had appeared. ✓ With the work of Ollier,⁹⁸ in 1859, in grafting bones from one animal into another, all the information necessary for the satisfactory repair of cranial defects was available. Several decades passed before it was used. ✓ Macewen⁷⁹ reported the reimplantation of antiseptic bone fragments into the cranial defects from which they were removed after the defect had been cleaned up and the fragments treated with bichloride of mercury. ✓ He had used this procedure since 1873 with fair success. ✓ The same year Buriel²⁰ and Guerix¹⁹ reported the implantation of bone buttons following trephining, Guerix on animals and Buriel on a human. The next year, Gerstein⁴⁴ used Macewen's method successfully in one case and Ballou⁵ described the satisfactory outcome of a case in which he reimplanted the trephine button. Senn,¹¹⁴ reporting on the use of antiseptic, decalcified bone to repair defects, made the statement that this method was excellent for the repair of cranial defects but gave no cases. The cases that he described all followed osteomyelitis elsewhere in the body.

✓Seydel,¹¹⁵ in 1889, reported a case of depressed fracture of the left parietal area in which, after the fragment had been removed, the defect was repaired by a graft several millimeters thick chiseled from the tibia with the periosteum intact. ✓ This graft was placed in saline, divided into pieces, and placed on the dura in a mosaic with the periosteum downward. The area was covered with a dry iodoform and bichloride dressing and then with silk. On the fifth day, the graft seemed healthy and closely adherent to the dura, the whole surface being pink. At this time the skin was closed. ✓ The patient made an uneventful recovery. With the report of this case the present day technics of plastic closure of the skull started. ✓ Von Jacksch⁶¹ felt that the drawback to Seydel's method was the necessity of two operations upon the same patient. He re-

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

ported a case in which a goose skull treated with ether and bichloride of mercury was used to fill in a cranial defect. The result was a solid, but slightly depressed, area.

✓ W. Muller,⁹⁴ in 1890, outlined a case in which he repaired a skull defect by taking a flap of skin, pericranium and outer table and swinging it into the defect in a manner similar to the old method for the reconstruction of the nose that had been known and used in India for centuries. ✓ König,⁹⁸ a little later in the same year, advocated the use of twin flaps. One flap contained the skin and what was left of the pericranium from the site of the defect and the other the skin, pericranium and outer table taken from an adjacent area in such a way that the bases of the flaps were opposite to each other and they might be transposed. ✓ The flap with the outer table then covered the defect and the skin flap filled in the area from which the outer table had been removed. The small openings left by the transposition of the flaps were closed by Tiersch grafts. This seemed to be a very adequate procedure for the repair of small defects but was not sufficiently elastic to be applicable to large ones. It is interesting to note that in this same paper he suggested that when trephining is necessary, a flap of skin, periosteum and outer table be formed. The trephine opening is made in the inner table and later covered with the outer table and skin as the flap is sewn back into place. This was probably suggested by the work of Wagner¹³⁴ (1889) on osteoplastic craniotomy.

✓ In 1891, von Hinterstoisser⁵⁸ reported a case of traumatic epilepsy with a cranial defect that he repaired with celluloid. Von Frey,⁴² in 1894, reported a case successfully closed with a celluloid plate and finally, in 1895, Fraenkel^{39, 40} reported his work on closing cranial defects with celluloid plates and cited three cases, one with a follow-up of three-quarters of a year, another died following the implantation of a celluloid plate in a wound that was infected before operation and not entirely healed at the time of the operation.

Kummell,⁷⁰ in 1891, made use of the method of Senn (1889), employing decalcified bone. He stated that he obtained good results but gives no statistics.

Schonborn,¹¹³ in 1891, reported a case done by König's method in which he was able to fill in a defect that measured 14x3 cm. A year later, Tietze¹²⁵ (1892) described a case in which he repaired a defect by König's method but gives very little information.

✓ In 1893, Booth and Curtis¹⁴ reported the first attempt to fill a cranial defect by means of a metal plate. They used aluminum. ✓ The patient died ten days after operation.

Beck,⁷ in 1894, outlined a case done by the König method and another done by a number of methods that all failed, although the patient finally had a spontaneous regeneration of bone. Czerny,²⁷ in 1895, reported that he had not had any success with celluloid plates, and that he had had trouble with one plastic of the König type because the patient had not had any diploe. One case done with a tibial graft was well after two years. One of the grafts introduced by the method of König had to be removed 18 months after operation.

for another cause. It was found that the graft had formed a new inner surface. In the same year, von Eiselberg³³ reported eight cases, in five of which he used the Muller-König technic. All were in good condition two years later. Of three that were done with celluloid, two were in good condition one and three-quarters and four and one-half years later, while one still had a fistula at the end of four years. He discusses the indications for this operation in cases of posttraumatic epilepsy, stating that although he had had no complete cures, most of the patients were benefited, some greatly, and that he feels it to be indicated in cases of focal epilepsy as well as in cases where pain is a large factor. Nicoladoni,⁹⁷ in 1895, reported a single case done with the Muller-König technic, which he modified by sawing the graft off after he had chiseled a groove around the area that he wished to remove. He felt that this avoided the cracking of the graft that occurs when it is removed with a chisel and gave a solid graft that was preferable.

✓ Gerster⁴⁵ (1895) repaired a defect of the skull with a thin gold plate. The case was followed for two and one-half years, at which time there was no demonstrable reaction to the metallic graft, and it was satisfactory in all ways.

Link⁷⁷ (1896) described three cases of celluloid cranioplasty, without adequate follow-up, and concluded that this method is advantageous for the closure of large cranial defects.

Berndt,⁹ (1898) reporting several cases done by the Muller-König or tibial graft technic, had been able to follow one case of tibial graft that was in excellent condition after six years.

Grekoff⁴⁷ (1898) used a technic developed by Baith⁶ (1896) in closing two defects with incinerated bone with apparent success, although the follow-up is not adequate.

✓ Von Hacker,⁵¹ in 1903, outlined a new method for the repair of defects. He cut around part of a pericranial flap, chiseled off the outer table under this flap, leaving it still attached to the flap, and then turned the flap over 180 degrees so that it came to lie over the defect with the bony side uppermost. He reported two cases done by this method and feels that it was applicable in many cases where the Muller-König method could not be used. ✓ In the same year, Bunge,¹⁹ in Garie's Clinic, reported two cases that were repaired by periosteal osseous flaps that were so placed that they could be swung into the defect without turning them over, thus leaving the periosteal side outermost, and stitching it to the surrounding pericranium. ✓ These cases were followed for 10 and 14 months and were solid and smooth when last seen. He also detailed the case of a patient whose defect was repaired by a fresh osteo-periosteal graft from another patient. The graft was good three years later.

✓ Keen,⁶⁸ in 1905, recommended the use of bone chips from the surrounding bone to fill in defects, and reported a case in which satisfactory repair was obtained in this way. ✓

✓ Stieda¹²² (1905) described eight cases that were adequately followed. Two patients had two operations. Six Muller-König cranioplasties were all in good condition at the end of periods varying up to five years. ✓ One showed

a small depression but it was solid. One case was cured of epilepsy. One repair, done by the von Hacker technic, was satisfactory for some time (?) following operation. One, done by the technic of Gaille, was in good condition after four years. One case, repaired with a piece of boiled bone, developed a fistula after nine months and was reoperated. The defect was repaired by a tibial graft. Five years later this was solid, though the patient complained of occasional headaches.

✓Blecher¹⁰ (1906) writing of celluloid cranioplasty, reported a case of his own and collected 11 from the literature, four of which had been unsuccessful. In the same year Borchard¹⁵ reported three cases of cranioplasty: one with the pericranium alone was unsuccessful, one with von Hacker's method with the periosteum innermost was solid but some spurs had developed over the graft. Eight cases of osteoperiosteal flap, after Gaille (Bunge), were all successful. Pingle¹⁰⁷ described six cases of celluloid cranioplasty, and found that they were unsatisfactory, one because of sepsis.

✓In 1907, Soh¹²¹ from Gaille's Clinic, reviewed their results to date and gives the work of Gaille in more detail. He reports seven cases in which various kinds of osteoperiosteal grafts were used. In five, either one or two flaps from the outer table of the skull were moved into the defect. In one case, the graft was cut entirely free from the pericranium and stitched into the defect—this is the earliest record that we find of this type of operation that is now in common usage. ✓One case was repaired by a separate osteoperiosteal graft of the outer table that was stitched into the defect with the bony side uppermost. ✓He states that Lyssenkow developed the technic of turning the graft 180 degrees so that the bony side was outermost and that von Hacker did this later. He quotes work by Durante that we have been unable to find in the literature up until 1922, although referred to by other authors without adequate reference.

• A case repaired with an aluminum plate was reported by Elsberg,⁸⁴ in 1908. ✓

Leotta,^{74, 75} in 1909, described a method that was adopted from Durante's technic of osteoplastic craniotomy. The whole thickness of the skin is taken, having attached to its under surface slivers of the outer table picked up by chiseling under the pericranium. The flap with these slivers attached is then freed at its base and displaced so that the portion containing the slivers of bone come to lie over the cranial defect. He states that one advantage of this technic is that it can be adapted to larger defects than the methods of von Hacker and Gaille.

✓Righetti^{108, 109} modified the methods of von Hacker and Durante by taking a periosteal flap with bone slivers attached and turning it 180 degrees to cover the defect. He reported five cases, using this method, that were in good condition from one month to six months after operation.

✓In 1916, Axhausen² returned to the osteoperiosteal graft from the tibia which he wedged into the defect with finger pressure. ✓His conclusions from 27 cases were that this method was better in every way than the Muller-König

Delagemiere²⁹ perfected the technic of osteoperiosteal grafts from the tibia, he cut his grafts thin and put them over the defect, between bone and pericranium with the periosteum outermost. Occasionally he used a second layer placed in the defect with the periosteum toward the dura so that both sides of the repaired area were smooth. In a number of papers, from 1916 to 1935,³⁰⁻³¹ he reported 104 cases with two failures, one of which was successfully reoperated.

In 1915, Morestin⁹⁰⁻⁹¹ described the use of cartilage for the repair of cranial defects. He took his grafts from other patients for the most part, and reported no difficulty arising because of this. A year later, Gosset⁴⁸ detailed 32 cases done by this method, in which there were two deaths, both from bronchopneumonia. He placed the perichondrial side innermost and held the graft in place by sutures. Other cases done with cartilage have been outlined by Auvray,¹ Leo,⁷¹ Peraire,¹⁰⁰ Villandre,^{127, 128} Laquiere,⁷¹ Chutro,²²⁻²³ Leiche,⁷⁶ Boinet,¹²⁻¹³ Gilmore,⁴⁶ Beguoin,⁸ Wilson,¹⁷⁶ Coughlin,²⁶ Hanson,⁵³⁻⁵⁴⁻⁵⁵ Munroe,⁹⁵ Julliard,⁶³ and Termier.¹²⁴

Mayet,⁸³⁻⁸⁴⁻⁸⁵⁻⁸⁶ in 1916, again used a method of osteoperiosteal graft from the skull, a flap that was turned 180 degrees and stitched in place by wire or catgut. He felt that this method was much easier than any of the others, and reported 43 cases without adequate follow-up. Cazin,²¹ the same year, operated upon 30 cases by a method in which he took a graft of skin, pericranium and outer table, or only pericranium and outer table, on a very long pedicle or with two pedicles and swung it into place with the bone side down. He states that the nourishment to this type of graft was adequate and probably better than that of the other methods.

Peraire¹⁰¹⁻¹⁰²⁻¹⁰³ (1916, 1917, 1919) described 29 cases done with various methods, and got good results in all of them.

Estot³⁶ (1916, 1917) reported 100 cases of cranioplasty with gold plates. Two cases died of infection and two were infected and the plate had to be removed. In the septic cases, the plates were found to be in good position and firmly fixed. He found the patients liked the gold plates.

Villandre,¹²⁷⁻¹²⁸⁻¹²⁹⁻¹³⁰⁻¹³¹ in a series of papers in 1916 and 1917, detailed 130 cases of cranioplasty done by different methods. He had his best results with osteoperiosteal grafts from the tibia. Less success followed in the cases that were repaired by placing calcium paste in the defect, hoping that the presence of the salts would act as a stimulant to new bone formation, as indeed was the case in half of the patients.

In reporting 10 cases of repair with osteoperiosteal flaps from the skull, Pflugradt¹⁰⁴ (1916) used the galea as part of the flap in four cases. The reason for this is not clear, unless it is that he used this method in larger flaps. One would think that the circulation of the skin would be badly interfered with, but his follow-up on these cases makes no note of this.

Westermann¹³⁵ (1916) recommended the use of the sternum as a graft for skull defects.

Babcock³ (1917) used soup bone to repair defects. He was able to follow two cases for two years, at which time they were in good condition. This

method had been used before by Villandie and others. Villandie reported 23 cases, with four failures, he used both human and animal bone.

✓ In 1917, Brown¹⁷ reported on the use of ribs in the repair of skull defects. He used only the outer half, leaving the inner half still in place. The notes on his cases are not adequate to judge his results, but here was a new method that gave promise of being very useful in the repair of large defects.

✓ In 1917, A. Hofman⁵⁹ modified the technic of osteoperiosteal flap grafting by cutting an extra large piece of periosteum, part of which he folded around the bone from the outer table. Just what he hoped to gain by this is not quite clear. The viability of the bone might be improved in this way, but it would seem to be an efficient barrier to any fusion of the graft to the edge of the defect. He gave no follow-up on any of his cases.

✓ Morrison⁹² (1917) reported 12 cases of tibia grafts in which the grafts were set into a slot cut in the edge of the cranial defect.

✓ In a series of papers by Siccard, Dambin and Rogei,^{117, 118, 119} from 1917 to 1919, and, later, Dambin and Dambin²⁸ (1936), the use of cadaver skull for cranioplasty was reported and 120 cases collected. The chief factors of importance were that they treated the bone with sodium carbonate and heat, then with xylol, then with alcohol and ether and finally sterilized it by heat. The bone was reduced in thickness until only the outer table remained and was then perforated freely. Their results were very satisfactory.

✓ In 1920, Kieider⁶⁹ described an interesting method of cranioplasty that has a limited scope. At the time of injury, he takes the fragments of bone removed from the depressed fracture and tucks them under the skin of the abdomen. Then at a later date, when the scalp wound has healed and the bone proven to be free from infection, he transplants it back into the defect.

MacLennan⁸⁰ (1920) detailed the use of parts of the scapula, noting that, by taking a piece from the infraspinatus fossa the full thickness of the bone, a graft is obtained that has periosteum on both sides and is still fairly thin. Saito,¹¹² in 1925, reported two cases done in this way. In 1921, Pickrell¹⁰⁵ described a similar technic using part of the ilium.

✓ Comoly²⁵ (1929) outlined the use of a platinum plate that stayed in place for 14 months without any sign of reaction. Luesma-Ulanga⁷⁸ (1936) reported the use of silver wire woven into a meshwork to fill in defects.

Fagasano,³⁷ in 1937, described the use of split ribs as grafts. He places them so that the normal curvature is inward regardless of which side the periosteum lays and places them in small slots in the bone, stitching them in place by using the pericranium.

Other authors who have used boiled or cadaver bone are Bonnet,^{11, 12, 13} Pankratiev,⁹⁹ and Guidjian.⁵⁰ Celluloid Blecher,¹⁰ Pringle,¹⁰⁷ and Eidheim.¹⁵ Fresh bone from other patients: Rocher,^{110, 111} Osteoperiosteal from the skull Le Fui,⁷² Frazier and Ingham,⁴¹ Coleman,²⁴ Dievermann,³² Sudhoff,¹²³ Bowei,¹⁶ Kafei,⁶⁵ Juvara,⁶⁴ Jones,⁶² and Guidjian.⁵⁰ Osteoperiosteal from the tibia Nesselrode,⁹⁶ Gilmore,⁴⁶ Begoun,⁸ Keil,⁶⁷ Rocher,¹¹⁰ Young,¹³⁷ Dievermann,³² Biusken,¹⁸ Terrier,¹²⁴ Hadley,⁵² and Fourmestiaux.³⁸ From

11bs Ballin,⁴ Shuttleworth,¹¹⁶ Biusken,¹⁸ and Gurdjian⁵⁰ Breast bone Mul-
lei, P⁹³ Ilium Money⁸⁹

It is not possible to analyze the cases in the literature as thoroughly as one might wish, because of the lack of adequate follow-up, which we think should be at least nine months and, better, a year. On the other hand, it seems to be true that most of the failures occur early and the shorter period will catch the majority of them. The cases in the charts do not include all of those that we have collected. We have eliminated all reports of single cases after 1900 unless they are important. A number of reports of a few cases have been left out because of lack of enough information to make them useful.

In all, we have charted 1,385 cases, arranged according to the method used, in an attempt to ascertain which of the various methods is the best. The only figure from the entire group that is at all significant is the mortality rate, which is 0.73 per cent.

Indications—There seems to be a happy accord among most of the authors as to the indications for cranioplasty and the only possible disagreement lies in the degree to which symptoms may be allowed to progress before operation is advisable. The indications are

- (1) Severe headache and other symptoms of the syndrome of the trephined—dizziness, undue fatigability, vague discomfort at the site of the defect, a feeling of apprehension and insecurity, mental depression and intolerance to vibration.
- (2) Epilepsy, when the attacks originated from the injury that caused the defect.
- (3) Those cases in which there is danger of trauma at the site of the defect.
- (4) Cases that have an unsightly defect.
- (5) Defects that pulsate unduly or that are painful.

The contraindications are again pretty well agreed upon. They are

- (1) The presence of any foreign body.
- (2) The presence of any possible infection in either brain or bone.
- (3) Increased cerebrospinal fluid pressure that is not easily reducible by lumbar puncture.
- (4) Pathologic changes in the cell count or chemistry of the fluid.

Cranioplasty should not be performed for some months after an injury unless the wound is undoubtedly clean. If there has been infection, it is not safe to attempt it in much less than one year's time. Some cases that have had osteomyelitis have given trouble several years after they were supposed to be free of infection. Delay allows the dura a chance to repair itself so that any infection at operation will remain extradural.

Among the authors who have written about the repair of cranial defects, Tuffier and Guillaum¹²⁶ have had the opportunity of following the greatest number of cases. They conclude that the procedure is of little value except from

the cosmetic point of view This opinion is at variance with that of the vast majority of writers

Technical Notes—There are several features apparent in reviewing the reported cases that are well accepted as important The scar of the original injury should be in good condition If it is not, there should be a preliminary operation to revise it and eliminate any danger of its breaking down from lack of an adequate blood supply or other cause A very thin scar should be revised even if adequately nourished When the defect is exposed, the dura should be well freed around the edge and any defects in it repaired by the use of fascial grafts Following this the bone edge should be freshened by cutting it back until healthy oozing bone is reached In cutting back the bone edge, the defect should be rounded as much as possible so that the graft will fit snugly While freshening the bone, the pericranium should be carefully protected so that it will be intact and in good condition to use in holding the graft in position The graft should be slightly larger than the trimmed defect to insure a snug fit If this is not done, the pericranium will adhere to the dura and form a barrier to bone formation between the graft and the edge of the defect If there has been any increase in intracranial pressure, great care must be taken to control it during the healing period, else it will lift the graft and prevent good bony union

Comparison of Methods—In general, it may be stated that the simplest methods are preferable and that methods entailing only one operative procedure are preferable to those necessitating two These factors are not, however, the only ones that demand attention, as we must consider the results, insofar as that is possible, of the different methods For example, it is well known, and admitted by all authors, that cranioplasties done with cartilage remain cartilaginous and the repaired area is never solid, but always has some "give" The fact that the cartilage is well tolerated (Beguoin,⁸ Chutro,²² and Moiestin⁹⁰), rarely absorbs (Chutio²²), and that it forms a firm union with the surrounding bone (Mariano and Virano⁸¹) is, for the moment, of little importance The important thing is that this method never brings about a firm, solid, bony closure, but tends to become more and more fibrocartilaginous as time goes on (Leriche⁷⁶) If this fact is accepted, and cartilage is reserved for the closure of small defects where the importance of a rigid graft is not so great, it has a very definite place in the operative scheme Its use for the closure of large defects is probably ill advised Furthermore, in the case of cartilage, if there is not a piece available from another patient—and it appears that cartilage from other humans is perfectly tolerated (Moiestin⁹⁰)—we are faced with the necessity of a second operation to obtain the graft But an osteoperiosteal graft from the external table of the skull, that may be either swung or thrown over into place, or taken separately and placed in the defect without connection with its original environment, will close it in a single operative session

The various types of osteoperiosteal grafts from the outer table of the skull all have their application in the repair of different sizes of defects depending somewhat on the location of the defect and on the condition of the overlying

skin It would seem to make little difference whether the bony or periosteal side of the graft is outermost, except that the bony side is more apt to be irregular Whether the graft remains attached to the pericranium by a pedicle is of no importance The possible blood supply from this source is poor at best, and we have had perfectly good results from grafts that were entirely separated from the pericranium

The work of Gallie and Robertson⁴³ has impressed us with the importance of using bone that has as much cancellous tissue as possible in order that many viable osteoblasts are available The diploic surface of the outer table of the skull seems to be a source for these, preferable perhaps to tibial grafts but probably not as good as rib grafts or grafts from the sternum The use of split ribs, especially in the repair of defects that are too large for a graft from the skull, is a very sound method The curvature of the pieces is just about right, and there are sufficient osteogenic cells present

The use of celluloid, we think, is to be avoided It is fairly well tolerated, but is objectionable on the following grounds Unless a fairly thick piece is used, it is not rigid and fails in its purpose Cases have been reported in which the graft has softened and become ineffective (Henschen⁵⁷) In this series is a case in which it was apparently the cause of severe headache and this has been reported by others (Pringle¹⁰⁷) The principal objection is that it is an unnecessary foreign body Further, it would seem that there are other foreign bodies that are better tolerated, such as gold (Eston³⁶), and which do not have the drawbacks of celluloid

An attempt to evaluate the results of cranioplasty insofar as the symptoms of the patients are concerned is very difficult The majority of the authors made no mention of the symptoms From the cases that were adequately followed and reported, we find that Stieda,¹²² out of eight cases, had two with occasional headaches, and one with vertigo and neuralgia of the supra-orbital nerve Auvray¹ reported one case that had headache and epilepsy five months after operation This case was reoperated upon by Villandre, and a ridge of cartilage was found pressing on the brain

Boinet¹¹ reviewed 41 cases of cranioplasty and 95 cases of cranial defect that had not been repaired and found that there were no significant differences between the symptomatology of the cases whose defect had been filled and those in whom it was still open It is, however, difficult to evaluate his figures accurately

Marie,⁸² in 1914, gave the details on 22 cases, six of whom were free of their symptoms or very much improved, 12 unchanged, and the remainder worse

Primrose¹⁰⁶ reviewed 42 cases, 19 of whom were cured of their complaints, eight improved, five unchanged, and two made worse Shuttleworth¹¹⁶ reported seven cases, four of whom were relieved of their complaints and two improved, while one was the same as before operation

Termier¹²⁴ was able to follow either personally or by letter some 63 cases that had been done 25 years before He felt that only a few epileptics or

psychotic patients had been improved, but that the majority of the triphine syndromes had been cured or greatly benefited. Fournestiaux³⁸ followed 15 cases for ten years. Eight were well and had no complaints, seven still had some complaints of greater or less severity.

One of the most interesting and at the same time most important features that enter into this problem is the effect of cranioplasty on convulsive states. It has been variously reported by König,⁶⁸ who had a cure following cranioplasty, von Eiselberg,³³ who had three cases that were better up to three years after the operation, Stieda,¹²² who had one cure and one unchanged, Mayet,⁸⁶ who had one cure, Chutio,²² who reported one case cured and one improved, Boinet,¹² who had four cases improved and three unchanged, and Dievermann,³² who had five cures and one improved out of 13 cases. Sudhoff¹²³ reported three cases that had epilepsy after but not before the operation. There have not been sufficiently accurate surveys to enable one to judge exactly the results of the operation. However, the majority of authors who have made any reference to epilepsy have reported that a certain number were either entirely relieved or improved. The cause of this and the mechanism behind it are not clear. Why, if a patient has convulsions following a cranial injury, does a repair of the cranial defect improve the convulsive state that must of necessity be due to the effect of the injury on the brain proper and not its coverings? The answer that immediately presents itself is that there is traction exerted on the brain by the overlying scalp. And it is perfectly true that following a cranioplastic repair the dura probably assumes a more normal position. It is still hard to see just how this helps a condition caused by cerebral cicatrix. The fact, however, remains that a small but very definite percentage of these cases are relieved of their convulsions following cranioplasty.

From 1911 to 1938, 89 operations directed toward the repair of cranial defects have been performed at the Hospital of the University of Pennsylvania, and at the Graduate Hospital of the University of Pennsylvania. In an attempt to evaluate cranioplasty and learn how much benefit may be derived from it, we have reviewed these 83 cases. Adequate follow-up examinations have been obtained in 58. In 25, roentgenologic examinations were made showing the conditions of the grafts at periods up to 19 years following operation. The follow-up examinations were, with very few exceptions, made by ourselves and most of the roentgenologic studies were made under the direction of the Roentgenologic Department of the University Hospital.

Indications—We were surprised to learn in going over the cases that the most frequent complaint was convulsive attacks. The other complaints in the order of their frequency are detailed in Table I.

It is often impossible to tell from the history the chief complaint of each patient and, therefore, just what was the indication for cranioplasty in each case. However, from the extensive histories of recent years, we feel that the syndrome of the triphined has not been a frequent indication for operation in either the early or later cases. All of these patients had cranial defects. It is surprising that only 13 came in for operation because of this alone.

TABLE I
SYMPTOMS

Convulsive state		54
Grand mal	24	
Focal attacks	27	
Petit mal (including "unconscious spells")	3	
Defect without other symptoms		13
Weakness or paralysis		13
Headache		12
Numbness and other sensory changes		11
Visual disturbances		9
Field defects	3	
Blurring or diplopia	6	
Mental changes		4
Speech disturbances		3
Painful or pulsating scar		4
		<hr/>
		123

The procedure that has been used in this clinic, almost to the exclusion of others, is a modification of the König-Müller operation that was developed by Dr C H Frazier in the early nineteen hundreds and has been used here practically unchanged since that time

TABLE II
TYPES OF CRANIOPLASTY

Osteoperiosteal graft from the outer table of the skull	75
Split rib graft with or without periosteum	7
Celluloid	2
Fascia only	2
Osteoperiosteal graft from the tibia	1
Osteoperiosteal graft from the scapula	1
Split bone flap	1
	<hr/>
	89

Operative Procedure—After the skin and galea are reflected to expose the defect, the pericranium is freed from its edge. The pericranium should be carefully preserved. The dura is then freed from the under surface of the bone. The edge is trimmed back with a chisel until healthy, oozing bone is encountered. The upper surface is beveled outward leaving a broad bearing surface for the graft to lie upon, and during the chiseling the contour of the defect is rounded out as much as possible. A pattern of this defect is now made of rubber tissue or any other suitable material. This pattern should be one-quarter of an inch larger than the defect all around. The skin incision is now extended or a new incision is made to expose an area of the skull where thick bone is usually found, such as the parietal eminence or the occipital region, and the pattern laid out here. The pericranium is cut around the pattern with a scalpel and along this line a groove in the bone is chiseled (Fig 1). Now, directing the chisel in this groove, nearly parallel to the surface of the

bone, the outer table is gradually cut through to the diploe and then by chiseling through this, the graft is finally cut free. Care must be taken not to go through the inner table or another defect will be made. If this is done, and it is occasionally impossible not to do it, the small defect should be filled with little bone chips. The thin graft is now taken and molded so that the pericranial side is convex instead of concave, as it is when removed. The graft is then fitted into the defect and the periosteum of the graft is tightly sutured to the periosteum surrounding the defect with interrupted sutures (Fig. 2). The graft should have been cut large enough so that there is a good area of bone approximation all around, otherwise the periosteum will become adherent to the dura and form a barrier to new bone formation between the

FIG. 1



FIG. 2



FIGS. 1 and 2 —The defect has been exposed and its edges freed from the pericranium and refreshed. A pattern of the defect is laid on an adjacent area of the skull, and the outer table, with its attached pericranium, is removed. The graft is then placed into the defect and the pericranium of the graft is sutured to the pericranium about the edges of the defect.

graft and the margin of the defect. The skin is closed with interrupted sutures in layers and drained for 24 hours.

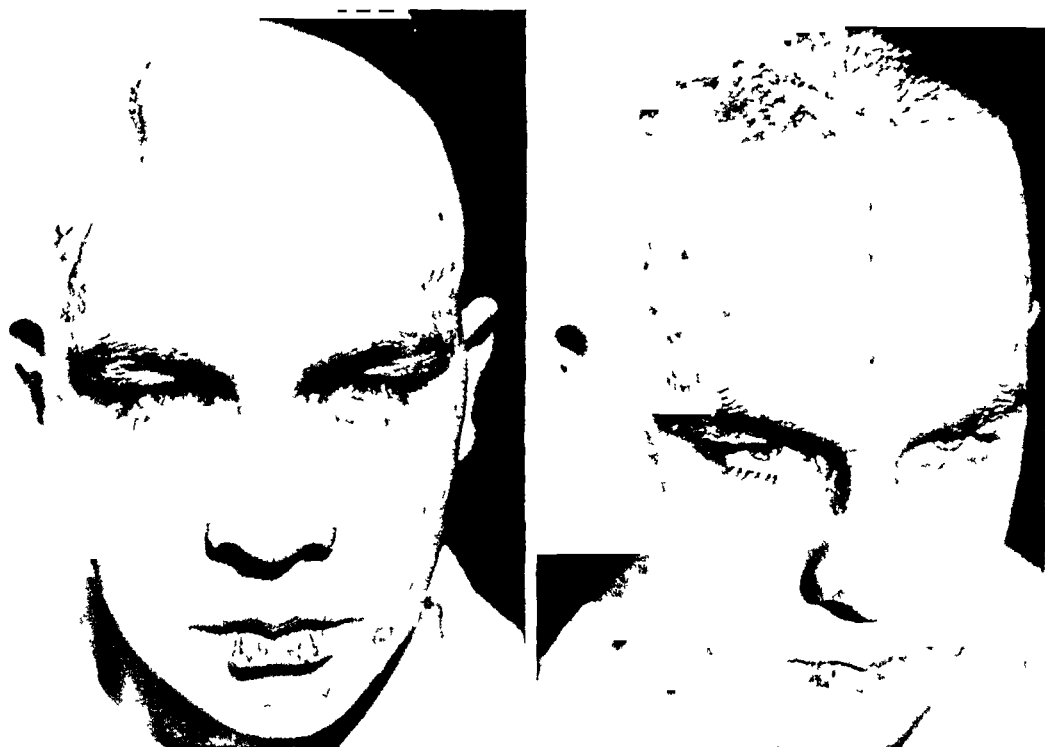
When the defect is larger than 6x6 cm., a split rib graft is the most satisfactory procedure. The ribs are exposed in the posterior axillary line. After the periosteum has been elevated, a piece of the proper length is resected. The ninth and tenth ribs suit the purpose very nicely. The ribs are then split by hand with a sharp, thin chisel so that two pieces, one concave and the other convex toward the cut surface, are available. These are placed in warm saline while the defect is exposed. This is done as for the other type of graft until the bone edge is trimmed. When using ribs the defect is shaped into a triangle or quadrilateral and a groove is cut in two opposing sides into which the ends of the ribs may rest and be secured. The pieces of rib are now fitted accurately into the prepared grooves and cut to fit snugly side by side regardless of whether the cut or smooth surface is uppermost. When the pieces are in place, the edge is marked and the grafts removed while holes are bored in the margin of the defect and in the ends of the ribs. Stainless steel sutures are put through these holes and the ribs wired in position. If there is any

play between the central parts of the ribs, more steel sutures are placed from rib to rib. The pericranium is now drawn up over the edges of the grafts as far as possible and tacked there with silk sutures. The galea and skin are closed with interrupted silk, as usual, and the wound is drained only if necessary. It has been our custom to aspirate any collection from under the skin flap, thus avoiding drainage whenever possible.

The techniques for the use of tibia, scapula, fascia and celluloid have been adequately described in the literature. We have not had enough experience with these types of repair to offer an opinion relative to them.

FIG 3

FIG 4



FIGS 3 and 4—Showing a patient before and after repair of a cranial defect

Patients are kept in bed for from five to seven days and are discharged in a week or ten days (Figs 3 and 4). The average stay in hospital of simple cranioplasty cases during the last seven years has been 14½ days.

Results—In the series of 83 cases having 89 operations, there were four postoperative deaths. Three of these cases had cortical excisions as well as cranioplasty, and the lateral ventricle was opened in two of them. The death following a simple cranioplasty was caused by postoperative meningitis. Of the other three cases, two died from infection and one from bronchopneumonia.

In addition to the simple cranioplasty, 14 cases had further surgical procedures directed toward the removal of bullets, excision of meningocerebral cicatrices, and the excision of a poencephalic cyst. For this reason these cases have been separated in evaluating the results from those having a simple cranioplasty.

REPAIR OF CRANIAL DEFECTS

Postoperative complications were seen in 15 patients (Table III). Only three of these cases were badly enough infected so that at least a part of the graft was lost or absorbed. The others recovered promptly.

TABLE III
POSTOPERATIVE COMPLICATIONS

Total cases	83
Deaths	4
Simple cranioplasty (infection)	
Cranioplasty and cortical excision	3
(2 infections, 1 bronchopneumonia)	1
Infections	8
With loss of graft	1
With loss of part of graft	1
With absorption of graft later	1
Outcome unknown	1
Superficial infections, grafts O K	4
Delayed healing	5
With serous drainage	3
With hematoma	1
Unknown cause	1
Pneumothorax	2
	—
Total	15

In the 58 cases that have been followed or examined, 48 show a satisfactory result as far as the plastic repair is concerned, from nine months to 19 years after operation. In a few cases there is a small depressed area in the center of the graft that does not pulsate, which in no way affects the efficiency of the graft, and does not give any trouble to the patient. Table IV summarizes the ten cases that are not considered satisfactory. Two cases show a small defect in the region from which the graft was taken. These defects are less than 1 cm in diameter and cause no symptoms.

TABLE IV
UNSATISFACTORY RESULTS OF 58 CASES FOLLOWED
9 MONTHS TO 19 YEARS

Absorption of graft	3
Depressed but solid	2
Graft depressible celluloid	2
(1 removed at later operation)	
Loss of graft following infection	3
(1 has a satisfactory fascial repair)	
	—
Total	10

In seven patients with grafts from the outer table, a subsequent operation was carried out that exposed the inner surface of the graft. One case was operated upon by Dr. Ira Cohen, of New York, to whom we are indebted for the following information: "The graft was well healed and solid. The inner surface was rough, extended below the surface of the surrounding inner table

and was adherent to the dura and through it to degenerated brain" (The patient had had a cortical excision at the time of the cranioplasty) The graft was removed in the hope that the release of the pressure would benefit his condition Six cases that were reoperated upon in our clinic (Figs 5, 6, 7 and 8), from one month to three years after cranioplasty, showed solidly healed grafts with irregular inner surfaces that projected very little beyond the inner surface of the skull The graft was adherent to the dura in all cases but was easily freed, and no note was made of there being any adhesions through to

FIG 5



FIG 6

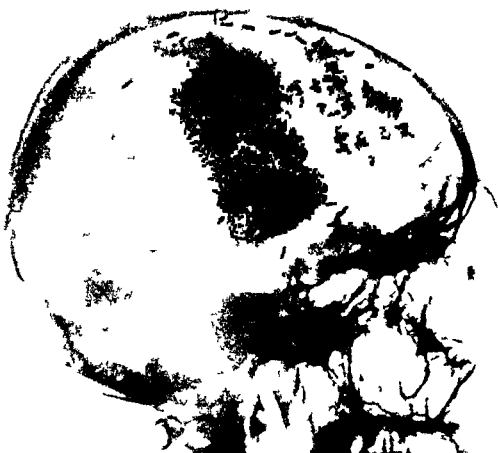


FIG 7



FIG 8

FIGS 5, 6, 7 and 8—In these two instances a bone flap was thrown about the repaired defect one year after cranioplasty had been performed Note that in spite of an area of decreased density, suggesting absorption of graft, the operative picture of the inside of the bone flap shows that the graft is entirely healed in and solid

the cerebrum In one case, there was a small area not covered in by bone where the pericranium had become adherent to the dura We feel that this case is important as it shows how a graft that is not approximated accurately might be unsatisfactory

In one case of a celluloid cranioplasty, the graft was removed because of severe and prolonged headache The celluloid was found to be enclosed in a sac formed by the pericranium and a bloodless, glistening membrane adherent to both pericranium and dura This membrane was several millimeters thick and was intimately connected with the dura from which it was peeled off in layers like an onion until healthy dura was reached The defect was repaired

REPAIR OF CRANIAL DEFECTS

with split ribs Examination two months later showed that the patient had been free from headache since the fifth postoperative day (Figs 9 and 10) Roentgenograms of grafts from the ninth month to the nineteenth year after

FIG 9

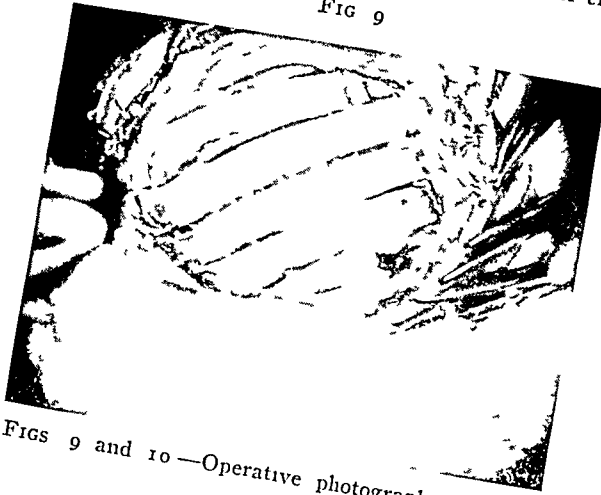
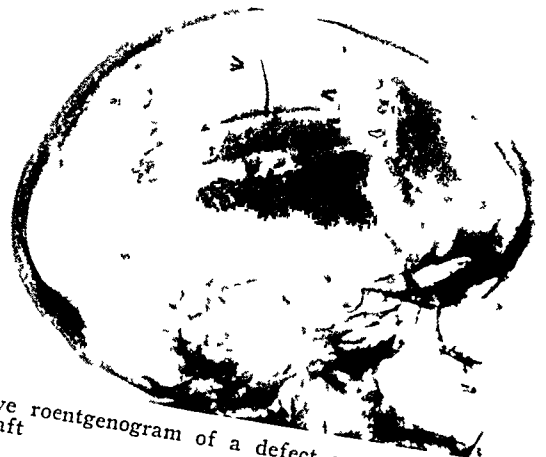


FIG 10



Figs 9 and 10—Operative photograph and postoperative roentgenogram of a defect repaired by use of split rib graft

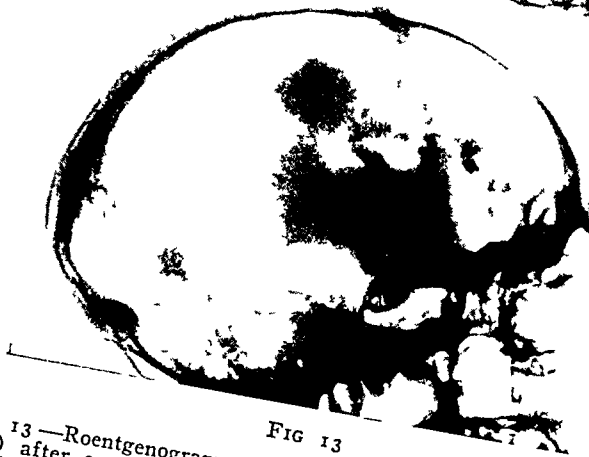
FIG 11



FIG 12



FIG 13



Figs 11, 12 and 13—Roentgenograms of repaired cranial defects 19 years (a), 11 years (b), and six years (c) after operation In spite of presence of apparent defect in the cranial vault the skull in each instance was entirely solid to palpation no pulsation could be seen and no posttraumatic clinical symptoms were present the operation yield a good deal of information (Figs 11, 12 and 13) One of the largest defects repaired by a graft from the outer table measured 6x13 cm at operation Figure 11 shows the roentgenographic appearance 19 years

later. There are many islands of bone in an area that is less dense and which might be a defect as far as one can tell from the roentgenogram. Examination of the area, however, shows it to be apparently solid bone without soft spots. The surface is irregular. The site of the removal of the graft is still visible in the roentgenograms but this too is solid to the examining finger. The appearance is rather typical of those found in other large defects. There appears to be a great difference in the thickness of the grafted bone or the new bone regenerated at the site of the graft.

This variability in the roentgenograms made their evaluation difficult. A local examination must be made at the same time to give the true result.

Two features in the roentgenogram of moderate sized grafts are noteworthy. First, there is frequently a less dense crescent around part of the

FIG 14



FIG 15



FIGS 14 and 15—Cranial defect and cranioplasty six months after repair. Note the thin line of decreased density about the edge of graft suggesting absorption. Graft entirely solid to palpation. No palpation could be seen or felt. Complete relief of clinical symptoms.

graft, that may or may not be ossified. Roentgenograms alone are unreliable and the area is too small to enable one to be sure from digital examination. Secondly, in some grafts the central portion is not as dense as the peripheral. This was true in the six cases that showed a small depression in the middle of the graft. In cases with this finding where a subsequent bone flap has been turned around the graft, no evidence of absorption of the graft has been seen. The graft seems to have healed readily into the surrounding bone.

A few generalities may be drawn from these roentgenologic studies. Healing in these grafts attains its maximum in less than a year, and thereafter little if any change can be demonstrated. In general it may be said that grafts in the frontal region will not bring about as thick a repair of bone as those in the posterior part of the skull. None of the grafts have shown any evidence of diploic formation and the grafts are for the most part thinner than the surrounding skull. The site of the removal of the graft remains visible for many years as a thinner area of bone.

Figures 14 and 15 show a patient who had a very satisfactory graft at the end of six months. Three months later the graft has for the most part absorbed and a pulsating defect is now present that is tenser than normal. The patient has intracranial hypertension from some, as yet unknown, cause.

REPAIR OF CRANIAL DEFECTS

TABLE V

SYMPTOMS FOLLOWING OPERATION

Cases with simple cranioplasty		58
Convulsive state		
Free of attacks for 8 mos , 2, 4, 16, 17, and 19 yrs	6	
One to 3 during postoperative period, then none for 9 mos , 1, 2, 7, and 18 yrs	7	
Attacks for 3 and 6 yrs, then free for 16 and 9 yrs	2	
Recurrence following another injury 8 mos and 3 yrs	2	
Free for 2 yrs , then spontaneous recurrence	1	18
Same after 1, 1½, 4, 5, 14, and 17 yrs	7	
Worse—died in status 2 yrs after	2	9
Total		27

TABLE VI

CASES WITH CRANIOPLASTY PLUS CEREBRAL EXCISION

Convulsive state		
Free of attacks for 1½ and 6 yrs	2	
One convulsion in 3½ yrs	1	
Better (attacks fewer and less severe) 1½, 1½, 2, 3, 6, 7, and 19 yrs	7	10
Same for ¾, 1, 1, 2½, 6, 7, and 18 yrs	7	
Worse—died in status 6 mos after	1	8
Total		18

TABLE VII

SYMPTOMS

		Good	Same
Cosmetic result satisfactory	7	7	
Cosmetic result failure (9 mos)	1		1
Painful defect satisfactory (4 and 18 yrs)	2	2	
Pulsating defect satisfactory (9 mos)	1	1	
Headache completely relieved (2, 4, 7, 7 and 16 yrs)	5	7	3
Less severe and frequent (1 and 18 yrs)	2		
Same (1 yr)	2		
Worse (case with celluloid plate 6 yrs)	1		
Dizziness relieved completely (6 and 16 yrs)	2	2	
Same (1 yr)	1		1
Weakness and paralysis (all but 2 had cerebral operations)		6	5
Nearly entirely relieved (7 yrs)	1		
Improved, strength and function (1½, 3, 3, 6 and 19 yrs)	5		
Same (1½, 1½, 2, 3, and 6 yrs)	5		
Visual disturbances Field defects all the same (3 mos , 1½, 2, and 5 yrs)	4		4
Numbness worse (1½ yrs)	1		1
Mental changes same after 1 yr	2		2
Better after 1½ yrs	1	1	
Totals	43	26	17

CONCLUSIONS

- (1) Simple cranioplasty has definite indications beyond the closure of a defect
- (2) Epilepsy is benefited by cranioplasty
- (3) The syndrome of the trephined is relieved in the large majority of cases
- (4) The cosmetic results of cranioplasty are excellent

BIBLIOGRAPHY

- ¹ Auvray, A Phenomenes de compression cerebrale observes a la suite de l'obturation d'une breche cranienne par un grand plaque de cartilage Bull et mem Soc de chir de Paris, 43, 2241, 1917
Idem Sur La Cranioplastie Bull et mem Soc de chir de Paris, 42, 1593, 1916
- ² Aukhausen, G Zur Technik der Schadelplastik Arch f klin Chir, 107, 551, 1916
- ³ Babcock, W W "Soup Bone" Implant for the Correction of Defects of the Skull and Face J A M A, 69, 352, 1917
- ⁴ Ballin, M A Method of Cranioplasty Surg, Gynec and Obstet, 33, 79, 1921
- ⁵ Ballou, W R Replacement of the Button of Bone after Trephining Med and Surg Rep, Philadelphia, 60, 198, 1889
- ⁶ Barth, A Uber kunstliche Erzeugung von Knochengewebe und uber die Ziele der Osteoplastik Berl klin Wchnschr, 33, 8, 1896
- ⁷ Beck, C Cranioplastic Operations J A M A, 23, 893, 1894
- ⁸ Begoun, P Cranioplasties Resultats eloignes Bull et mem Soc med et chir, Bordeaux, 88, 1921
- ⁹ Berndt, F Uber den Verschluss von Schadeldefekten durch Periostknochenlappen von der Tibia Deutsch Ztschr f Chir, 48, 620, 1898
- ¹⁰ Blecher Uber die heteroplastische Deckung von Schadeldefekten mit Zelluloid Deutsch Ztschr f Chir, 82, 134, 1906
- ¹¹ Boinet Suites comparees des Cranioplasties et des brches osseuses craniennes sans plastie Marseille Med, 55, 493, 1918
- ¹² Boinet Nouveaux cas de cranioplasties Marseille Med, 55, 552, 1918
- ¹³ Boinet Bieches avec plasties craniennes Marseille Med, 56, 182, 1919
- ¹⁴ Booth, J A, and Curtis, B F Report of a Case of Tumor of the Left Frontal Lobe ANNALS OF SURGERY, 17, 127, 1899
- ¹⁵ Borchard Zur subaponeurotischen Deckung von Schadeldefekten nach v Hacker-Durante Arch f klin Chir, 80, 642, 1906
- ¹⁶ Bower, J O Management of Injuries to the Cranium and Its Contents ANNALS OF SURGERY, 78, 433, 1923
- ¹⁷ Brown, R C The Repair of Skull Defects Med Jour Australia, 11, 409, 1917
- ¹⁸ Brusken Frei Knochenplastik bei Schadeldefekten nach Schussverletzungen Arch f klin Chir, 128, 448, 1924
- ¹⁹ Bunge Uber die Bedeutung traumatischer Schadeldefekte und deren Deckung Arch f klin Chir, 71, 813, 1903
- ²⁰ Burrel, H L The Reimplantation of a Trephine Button of Bone Boston Med and Surg Jour, 118, 313, 1888
- ²¹ Cazin De la cranioplastie par glissement au moyen de lambeaux osseux pedicules Paris Chir, 9, 102, 1917
- ²² Chutro, P Resultats de la cranioplastie Bull et mem Soc de chir, Paris, 48, 481, 1917
- ²³ Chutro, P Cartilagenous Cranioplasties Internat Jour Surg, 32, 227, 1919
- ²⁴ Coleman, C C The Repair of Cranial Defects by Autogenous Cranial Transplants Surg, Gynec and Obstet, 31, 40, 1920

- ²⁵ Cornioly, C Apropos de la Cranioplastie Rev méd de la Suisse, 49, 677, 1929
- ²⁶ Coughlin, W T Cranioplasty with Cartilage Surg Clin North Amer, 2, 1627, 1922
- ²⁷ Czerny Dreiplastische Operationen Verhandl d Deutsch Ges f Chir, 24, 13, 1895
- ²⁸ Damorin, L P Les plasties craniennes par homoplaques osseuses sterilisees Bordeaux Chir, 7, 279, 1936
- ²⁹ Delagemere, H Les greffes osteopériostiques prises au tibia Bull et mem Soc med et chir, Bordeaux, 42, 1048, 1916
- ³⁰ Delagemere, H A General Method of Repairing Loss of Bony Substance and of Reconstructing Bones by Osteoperiosteal Grafts Taken from the Tibia Surg, Gynec and Obstet, 30, 441, 1920
- ³¹ Delagemere, H Symposium Bull et mem Soc de chir de Paris, 42, 1593, 1916
- ³² Drevermann, P Uber den Ersatz von Dura und Schiadeldefekten Beitr f klin Chir, 127, 674, 1922
- ³³ v Eiselberg, F Zur Behandlung von ernobenen Schadelknochendefekten Beilage z Zentralbl f Chir, 22, 44, 1895
- ³⁴ Elsberg, C A Plate for Defects of the Skull ANNALS OF SURGERY, 47, 795, 1908
- ³⁵ Erdheim, S Zur Deckung von Schadeldefekten mit Zelluloidplatten nach Fraenkel Zentralbl f Chir, 66, 858, 1933
- ³⁶ Estor, E Cent cas de prothese cranienne par plaque d'or Bull et mem Soc de chir de Paris, 48, 463, 1917
Idem Symposium Bull et mém Soc de chir de Paris, 42, 1593, 1916
- ³⁷ Fagarasão, J Procedé de cranioplastie par des greffons costaux redoubles Tech chir, Paris, 29, 57, 1937
- ³⁸ Fourmestrau\ Resultats eloignes de la cranioplastie par greffon ostéopériostiques, P verb Congr franc chir, 37, 857, 1928
- ³⁹ Fraenkel, A Uber Heteroplastik bei Schadeldefekten Arch f klin Chir, 1, 407, 1895
- ⁴⁰ Fraenkel, A Uber Heteroplastik bei Schadeldefekten Beilage z Zentralbl f Chir, 22, 47, 1895
- ⁴¹ Frazier, C H, and Ingham, S D A Review of the Effects of Gunshot Wounds of the Head Trans Amer Neuro Assoc, 1919, pp 59
- ⁴² v Frey Uber Einheilung von Celluloidplatten Wein klin Wchnischr, 7, 40, 1894
- ⁴³ Gallie, W E, and Robertson, D E The Transplantation of Bone J A M A, 20, 1134, 1918
- ⁴⁴ Gerstein Uber Verschluss von Defekten am Schadel mit Demonstration Verhandl d Deutsch Ges f Chir, 18, 89, 1889
- ⁴⁵ Gerster, A G Heteroplasty for Defect of the Skull Trans Amer Surg Soc, Philadelphia, 13, 485, 1895
- ⁴⁶ Gilmore, C M The Transplantation of Bone in the Repair of Cranial Defects Surg, Gynec and Obstet, 27, 311, 1918
- ⁴⁷ Grekoff, J Uber die Deckung von Schadeldefekten mit ausgegluhten Knochen Zentralbl f Chir, 25, 969, 1898
- ⁴⁸ Gosset, A Symposium Bull et mem Soc de chir de Paris, 42, 1593, 1916
- ⁴⁹ Guerix, M A Reimplantation des roundelles osseuses apres la trépanation Bull de l'Acad de med, 20, 604, 1888
- ⁵⁰ Gurdjian, E S Management of Depressed Fractures of the Skull and Old Skull Defects ANNALS OF SURGERY, 102, 89, 1935
- ⁵¹ v Hacker Ersatz von Schadeldefekten durch unter der Kopfschwartz verschobener oder un gelappte Periostknochen Beitr z klin Chir, 37, 499, 1903
- ⁵² Hadley, F A Skull Defects Repaired by Tibial Grafts Jour Col Surg Australia, 1, 208, 1928-1929
- ⁵³ Hanson, A M The Costochondral Graft for the Repair of Skull Defects Minnesota Med, 7, 610, 1924, Mil Surg, 48, 691, 1921
- ⁵⁴ Hanson, A M The Restoration of the Internal Table in Cranioplasty Mil Surg, 50, 31, 1922

- ⁵⁵ Hanson, A M The Care of Injuries of the Brain in War and the Value of Costochondrial Grafts in Skull Defects *Mil Surg*, 74, 61, 1934
- ⁵⁶ Henschen, K Subaponeurotische Deckung grosser Schadeldefekte mit gewobten Hornschalen *Beitr f klin Chir*, 99, 559, 1916
- ⁵⁷ Henschen Quoted from Dievermann⁵² Uber den Ersatz von Dura und Schadeldefekten *Beitr f klin Chir*, 127, 674, 1922
- ⁵⁸ v Hinterstoisser Uber einen durch Tripanation geheilten Fall von traumatischer Epilepsie (Jackson) nebst Bemerkungen zur Heteroplastik mittelst Zelluloid *Wien klin Wchnsch*, 1891
- ⁵⁹ Hofmann, A Zur Technik der Schadelplastik *Zentralbl f Chir*, 44, 25, 1917
- ⁶⁰ Hoffman, E Uber der Deckung von Schadeldefekten *Deutsch med Wchnsch*, 42, 783, 1916
- ⁶¹ v Jacksch, R Zur Frage der Deckung von Knochendefekten des Schadels nachs Trepanation *Wien med Wchnsch*, 39, 1436, 1889
- ⁶² Jones, R W The Repair of Skull Defects by a New Pedicle Bone Graft Operation *Brit Med Jour*, 1, 780, May, 1933
- ⁶³ Julliard Les Suites eloignes des cranioplasties cartilagineuses *P verb Congr franc chir*, 37 841, 1928
- ⁶⁴ Juvara Procédé de cranioplastie reconstruction de la paroi *Rev de chir*, Paris 71, 401, 1933
- ⁶⁵ Kafel, H Uber das Schicksal nach v Hacker-Durante plastischgedeckter Schadelverletzter *Arch f klin Chir*, 128, 629, 1924
- ⁶⁶ Keen, W W Filling Defects of the Skull by Bone Chips from the Outer Table of the Neighboring Bone *ANNALS OF SURGERY*, 42, 296, 1905
- ⁶⁷ Kerr, H H Osteoperiosteal Graft of Delagenerie But with Bone Surface Inward *Surg, Gynec and Obstet* 30, 550, 1920
- ⁶⁸ König, F Der knocherne Ersatz grosser Schadeldefekte *Zentralbl f Chir*, Leipzig, 17, 497, 1890
- ⁶⁹ Kreider Repair of Cramal Defects by a New Method *J A M A*, 74, 1024, 1920
- ⁷⁰ Kummell Uber Knochenimplantation *Deutsch med Wchnsch*, 17, 389, 1891
- ⁷¹ Laquiere Cranioplasties cartilagineuses *Lyon med*, 126, 138, 1917
- ⁷² Le Fui Technique operationne et resultats de la cranioplastie osseuse *Presse med*, Paris, 26, 18, 153, 1918
Idem Seize cas de cranioplastie avec succes *Paris chir*, 9, 156, 1917
- ⁷³ Leo, G Cranioplastie cartilagineuse dans les pertes de substance cranienne *Paris chir*, 8, 278, 1916
- ⁷⁴ Leotta, N Verfahren der Knochenautoplastik zur Ausfullung von Substanzverlusten der Schadelknochen *Deutsch Ztsch f Chir*, 103, 147, 1900
- ⁷⁵ Leotta, N Processo di autoplastica ossea per colmare perdite di sostanza della ossa craniche *Bull del Accad Real med di Roma*, 38, 179, 1910
- ⁷⁶ Leriche, R Etude histologique de deux cas de greffe cartilagineuses *Lyon chir*, 14, 916, 1917
- ⁷⁷ Link, I Casuistische Beitrage zu Heteroplastik beim Schadeldefekten mit Zelluloidplatten nach Fraenkel *Wien med Wchnsch*, 46, 950, 1896
- ⁷⁸ Lluesma-Ulanga, E Las filigranas de hilo de plata en cranioplastia *Rev cir Barcelona*, 11, 155, 1936
- ⁷⁹ Macewen On the Surgery of the Brain and Spinal Cord *Med News*, Philadelphia, 53, 169, 188
Idem *Lancet*, 2, 254, 1888
- ⁸⁰ MacLennan, A The Repair by Bone Graft of Gaps in the Skull Due to Congenital Deficiency, Injury or Operation *Glasgow Med Jour*, 93, 251, 1920
- ⁸¹ Mairano, M, and Virano, G Cranioplastica con autotripananti di cartilagine elastiche *Clin Chir*, Milan, 32, 1687, 1929
- ⁸² Marie, P Symposium *Bull et mem Soc de chir de Paris*, 42, 1593, 1916

- ⁸³ Mayet Restauration des pertes de substance cranienne par rabattement volet osteo-periostique Bull Acad med, Paris, 75, 157, 1916
- ⁸⁴ Mayet Obliteration des pertes de substance cranienne par rabattement d'un volet osseux empiunte a la table externe de la region cranienne voisine Paris chir, 8, 105, 1916
- ⁸⁵ Mayet Cranoplastie Paris chir, 8, 451, 1916
- ⁸⁶ Mayet Resultats eloignes de la cranioplastie par le procede de la charniere Paris chir, 9, 58, 1917
- ⁸⁷ Mayet Cranioplastie par le procede de charniere Paris chir, 9, 152, 1917
- ⁸⁸ Mertens, V E Experimentelle Beitrage zur Frage der knochern Deckung von Schadeldefekten Deutsch Ztschr f Chir, 57, 518, 1900
- ⁸⁹ Money, R A Osteoplastic Restoration of the Skull Med Jour Australia, 19, 269, 1932
- ⁹⁰ Morestin, H Les transplantations cartilagineuses dans la chirurgie reparatrice Bull et mem Soc de chir de Paris, 41, 1994, 1915
- ⁹¹ Morestin, H Symposium Bull et mem Soc de chir de Paris, 42, 1593, 1916
- ⁹² Morrison, A E Autoplastic Transplantation of Bone in Injuries of the Skull Brit Jour, Surg, 1917
- ⁹³ Muller, P Über die Verwendug des Brustbeins zur Schadeldefektdeckung und ihre Erfolge Beitr z klin Chir, 14, 651, 1918
- ⁹⁴ Muller, W Zur Frage der temporären Schadelresektion an Stelle der Trepanation, Zentralbl f Chir, 17, 65, 1890
- ⁹⁵ Mumoe, A R The Operation of Cartilage Cranioplasty Canad Med Assoc Jour, 14, 47, 1924
- ⁹⁶ Nesselrode, C C Closure of Cranial Defects by Osteo-periosteal Grafts Taken from the Tibia Surg Clin North Amer, 3, 789, 1919
- ⁹⁷ Nicoladoni Modification der König'schen Knochenplastik Beilage z Zentralbl f Chir, 22, 44, 1895
- ⁹⁸ Ollier, L De la production artificielle des os au moyen de la transplantation de perioste et des greffes osseuses Gaz med de Paris, 30, 226, 1859
- ⁹⁹ Pankratiev, B E Dead Bone Grafts to Repair Skull Defects ANNALS OF SURGERY, 97, 321, 1933
- ¹⁰⁰ Peraire, M Cranioplastie cartilagineuse Paris chir, 8, 515, 1916
- ¹⁰¹ Peraire, M Cranioplastie au moyen du procede Mayet Paris chir, 8, 651, 1916
- ¹⁰² Peraire, M Cranioplastie par le procede de la charniere Paris chir, 9, 118, 9, 135, 9, 186, 9, 346, 1917
- ¹⁰³ Peraire, M Des procedes autoplastiques pour obliteration les breches de la voute du crane, critique et statistique generale Paris chir, 11, 221, 1919
- ¹⁰⁴ Pflugradt Über Schadeldefekte Beitr z klin chir, 103, 465, 1916
- ¹⁰⁵ Pickerill, P A New Method of Osteoplastic Restoration of the Skull Med Jour Australia, 18, 228, 1921
- ¹⁰⁶ Primrose, A Cranioplasty The Value of a Graft of Bone, Cartilage or Fascia in the Closure of Cranial Defects Caused by Wounds in War ANNALS OF SURGERY, 70, 1, 1919
- ¹⁰⁷ Pringle, J H Remarks on the Closure of Gaps in the Skull Brit Med Jour, 1, 246, 1906
- ¹⁰⁸ Righetti, C Autoplastica ossea del cranio Clin chir, Milano, 17, 1097, 1909
- ¹⁰⁹ Righetti, C Sul modo di riparare perdite di sostanza ossea del cranio Clin chir, Milano, 20, 2237, 1912
- ¹¹⁰ Rocher Reflexions a propos de trois nouveaux cas de cranioplastie resultats eloignes post-operatoires d'un serie de 43 cranioplasties (Delagemeire) Gaz Soc Med Bordeaux, 42, 505, 1921
- ¹¹¹ Rocher Cranioplastie pour pertes de substance cranienne Bull et mem Soc med et chir, Bordeaux, 23, 396, 1923-1924

- ¹¹² Saito, M. Über Kramioplastik. Arch f klin Chir, 119, 321, 1922
- ¹¹³ Schonborn. Knocherner Ersatz eines grossen traumatischen Schadeldefektes nach der Methode von König. Arch f klin Chir, 42, 808, 1891
- ¹¹⁴ Senn, N. On the Healing of Antiseptic Bone Cavities by Implantation of Antiseptic Decalcified Bone. Am Jour Med Sci, N S, 98, 219, 1889
- ¹¹⁵ Seydel. Eine neue Methode, grosse Knochendefekten des Schadels zu Deckung. Zentralbl f Chir, 16, 209, 1889
- ¹¹⁶ Shuttleworth, C B. The Repair of Bony Defects of the Cranium. Canad Med Assoc, Jour, 11, 562, 1921
- ¹¹⁷ Siccard, J A, and Dambrin, C. Plastie du crane par os humain sterilize. Presse med, Paris, 25, 60, 1917
- ¹¹⁸ Siccard, J A, Dambrin, C, and Roger, H. Plastie du crane par plaque osseuse homologue. Marseille Med, 15, 117, 1918
- ¹¹⁹ Siccard, J A, Dambrin, C, and Roger, H. Contrôle autopsique d'une plastie osseuse cranienne. Marseille Med, 55, 564, 1918
- ¹²⁰ Siccard, J A, and Dambrin, C. Resultats eloignes des cranioplasties par homoplaque osseuse cranienne. Rev Neurol, 35, 517, 1919
- ¹²¹ Sohr, O. Zur Frage der Schadelplastik. Beitr z klin Chir, 55, 465, 1907
- ¹²² Stieda, A. Beitrage zum Frage der Verschluss traumatische Schadeldefekte. Arch f klin Chir, 77, 532, 1905
- ¹²³ Sudhoff, W. Zur Kasuistik und Statistik der Schadelschusse im Heimaltazarett. Deutsch Ztschr f Chir, 179, 289, 1923
- ¹²⁴ Termier. Indications et suites eloignes de la cranioplastie. P verb Congr franc chir, 37, 854, 1928
- ¹²⁵ Tietze, A. Über den Osteoplastischen Verschluss von Schadeldefekten. Arch f klin Chir, 45, 227, 1892-1893
- ¹²⁶ Tuffier, T, and Guillain, C. The Treatment of Secondary Complications of Head Injuries. Arch de Med et Pharm, 69, 263-287, 1918
- ¹²⁷ Villandre, Ch. Technique operatoire de la cranioplastie cartilagineuse. Presse med, Paris, 24, 399, 1916
- ¹²⁸ Villandre, Ch. La cranioplastie cartilagineuse. Lyon Med, 125, 405, 1916
- ¹²⁹ Villandre, Ch. Reparation cranienne par plaques osseuses. Lyon Med, 126, 140, 1917
- ¹³⁰ Villandre, Ch. Reparation des pertes de substance cranienne. Presse med, Paris, 25, 301, 1917
- ¹³¹ Villandie, Ch. Technique de la reparation des pertes de substance cranienne. Presse med, Paris, 25, 540, 1917
- ¹³² Villandre, Ch. Reparations craniennes, leur indications, le choix des procedes, les resultats. Rev de Chir, Paris, 54, 184, 1917
- ¹³³ Villandre, Ch. Repair of Loss of Substance in the Cranium. Med Presse, London, N S, 105, 429, 1918
- ¹³⁴ Wagner, W. Die temporare Resektion des Schadeldaches au Steele der Trepanation. Zentralbl f Chir, 16, 833, 1889
- ¹³⁵ Westermann, C W J. Zur Mathodik der Deckung von Schadeldefekten. Zentralbl f Chir, 43, 113, 1916
- ¹³⁶ Wilson, G E. The Repair of Cranial Defects. ANNALS OF SURGERY, 69, 230, 1919
- ¹³⁷ Young, R F. Case of Cranial Injury and Cranioplasty. Glasgow Med Jour, 97, 63, 1922

DISCUSSION —DR WILLIAM JASON MIXTER (Boston) I think the subject considered by Doctor Grant a very valuable one to have brought up to date at the present time, because the literature has been full of various articles covering parts of this material

I should agree absolutely with his idea that the outer table graft is the

graft of choice, where it can be used. It is interesting to examine one of these grafts later when one turns down a bone flap including the graft, and to see that the graft has definitely thickened in a year or two.

In speaking of the various foreign materials, I agree with what he says about celluloid. Celluloid frequently causes a definite reaction about it. I operated upon one case that had had a gold plate put in nearly 20 years before. It was very interesting to compare the result in that case with the celluloid cases which have been reexplored. The gold plate apparently had stimulated absolutely no tissue reaction about it.

There is one thing that Doctor Grant did not mention, although I know that he uses it, because I have seen his cases, and that is that these patients must have a firm, protective dressing outside, in order that the graft may not be knocked in accidentally while the patient is asleep, during the first few days or weeks after operation.

There is one other point, and that is that where a patient has a depressed fracture, instead of lifting the depressed fragments, it is sometimes easier to take out the whole depression and turn it over, using the curve of the depression to match the curve of the skull.

DR. HOWARD C. NAFFZIGER (San Francisco). The most interesting and surprising point in Doctor Grant's presentation is the very high percentage of cures or improvement in convulsive states after simple repair of the bony defect, without resection of the brain scar. I had no idea that it would be so high.

We have performed many cranioplasties of the type that Doctor Grant recommends. It has certain obvious advantages, particularly in having only one field of operation exposed. Although I am unable to give our statistics, we have been disappointed by having the graft absorbed in a larger percentage of cases than he has, I am sure. That does not mean, necessarily, that the defect is as unprotected as it was before, because even in those instances in which absorption occurred, the defect was filled in by a heavy fibrous covering that gave adequate protection.

We have not been pleased with the results obtained by using foreign materials. There is one form of graft that we feel gives better cosmetic results than others and which we like for that reason. We have used it only recently. In one patient it was necessary to sacrifice a bone flap in the frontal area because of a meningioma which had invaded the sinuses extensively. We were anxious to secure a particularly good cosmetic result and, as one of our orthopedic associates is particularly skillful in removing grafts from the pelvis, we used grafts from the innominate bone. These can be chosen with reference to their curvature and can be removed with saw and chisel. They can be perfectly adapted in size and shape and give a better cosmetic result than any other type.

I think that possibly I have been a little prejudiced against extensive removals of bone from the skull by chisel, because of the necessity for the use of the hammer and the jarring it produces.

Any of the autografts may absorb. I had the opportunity of following the course of one patient for 22 years—from 1915 to 1937. A tremendous loss of bone from the frontal area was repaired with strips of osteoperiosteal grafts from the tibia, which gave an excellent cosmetic result. In roentgenograms, the grafts seemed to be unchanged for some five or six years, and then successive films showed that the strips of bone were becoming less and less dense and finally, at the end of something over 20 years, they could no longer be seen, the cosmetic result, however, was almost as satisfactory as in the beginning. The graft seemed to have been replaced by a very heavy fibrous covering.

DR FRANCIS C. GRANT (closing). I am glad Doctor Mixter brought up the point of the postoperative protective dressing. I think it is very important. We incorporate a lead plate inside the bandage of sufficient size to overlap the defect, and that certainly prevents difficulty during the ten days the patient remains in the hospital, and after their discharge we fit them out with an aluminum protector which they wear for three months. That goes around the head and has a rubber band on it which holds it in place, and they are supposed to wear that pretty constantly during the next three months.

I was interested in what Doctor Naffziger said about the innominate bone. We have not used that. I do not see why it would not be a thoroughly satisfactory method for repairing a cranial defect.

As far as the gradual absorption of bone is concerned, I feel quite certain that that occurs, although we base that particularly on the roentgenologic appearance, and, when we studied these patients later, by actual palpation, and examination of the graft, it was amazing the way in which the roentgenograms had overestimated the condition of the graft. Those grafts are really in first-class shape. You could tap on them with your knuckle, and apparently they are just as hard as any other part of the patient's head, although roentgenologically they certainly looked as though a great amount of absorption had occurred.

We have been thoroughly satisfied with this procedure, and I see no reason from this study to change our opinion about it.

EXPERIENCES WITH THE TOTAL AND INTRACAPSULAR EXTIRPATION OF ACOUSTIC NEUROMATA*

GILBERT HORRAX, M D , AND JAMES L POPPEN, M D

BOSTON, MASS

FROM THE NEUROSURGICAL SERVICE OF THE LAHEY CLINIC, NEW ENGLAND DEACONESS AND
NEW ENGLAND BAPTIST HOSPITALS, BOSTON, MASS

THE LIFE HISTORIES of many individual types of brain tumor, some of which are situated in a specific and well-known region of the intracranial cavity, have been worked out during the past quarter of a century, during which neurologic surgery has made such significant advances. It is now possible before operation not only frequently to recognize what type of growth one is dealing with, together with its exact situation, but also to predict with a fair degree of accuracy what the operative dangers will be as well as the future life expectancy and usefulness of the patient. Among the intracranial tumors to which these statements apply, the acoustic neuromata (the common cerebellopontile angle tumors) should probably be given the first place. The story of their recognition and the early surgical attacks upon them, their persistent resistance to complete extirpative methods, and their final capitulation, forms a long, but fascinating, although at times gruesome, chronicle in the annals of surgical advance.

It is not pertinent to the subject of this paper to retell this story which has been related so well by others, notably Cushing¹ and Dandy.² A few of the outstanding milestones, however, must be noted in order to get a proper background, and, therefore, some understanding of the difficulties pertaining to the enucleation of these growths, which, though entirely benign and encapsulated, are, nevertheless, so hemmed in by vital structures that their removal is attended with the greatest hazard.

Descriptions of the pathology of acoustic tumors go back to the latter part of the eighteenth century, and scattered clinical records are to be found through the early part of the nineteenth, notably that of Cruveilhier.³ Their localization and clinical recognition had become fairly well established during the early years of the present century, following the advances made in cerebral and cerebellar localization.

Along with the earliest clinical localizations came an occasional surgical attempt at removal of these tumors, with a still more occasional successful result. Indeed, it is a matter of considerable wonder that any patient should have survived the operation as carried out at that time, namely, a quick, finger enucleation of the tumor with inevitable severe trauma to the brain stem and to the many cranial nerves and large blood vessels in the region. It must be borne in mind, however, that surgeons in that era were just beginning to acquire a knowledge of how to attack lesions of the brain and spinal cord and had

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

none of the modern adjuncts which we now regard as absolutely essential for this branch of surgery

It is not surprising, therefore, that when the operative statistics concerning acoustic neuromata were brought to light at the International Congress of Medicine in London, in 1913, the mortality was so prohibitive as to make surgery seem well-nigh hopeless. Tooth's⁴ report from the National Hospital at Queen Square, London, showed a 58 per cent mortality in the cases presumably operated upon by Sir Victor Horsley, and of the 12 patients it is probable that only one of the five survivors may have had a complete extirpation. The story from continental Europe at the same Congress was even worse, von Eiselsberg reporting 12 deaths in 16 cases, an operative mortality of 75 per cent, and Krause 26 deaths in 31 cases, an 83.8 per cent mortality rate. From both of these series it is fair to assume from the records that only one (a patient of von Eiselsberg's) survived for any prolonged useful period.

The first notable advance from this desperate situation in the surgical treatment of acoustic tumors came with the publication, in 1917, of Cushing's monograph on Tumors of the Nervous Acousticus.¹ In this work the method of intracapsular enucleation of the tumor was described, and although admittedly not an ideal operation for a benign, encapsulated lesion, nevertheless a patient was, for the first time, offered a procedure which carried a relatively low mortality (20 per cent at that time), relief from pressure symptoms and, not infrequently, rehabilitation to useful life for perhaps two to eight years. In a subsequent publication,⁵ in 1932, Cushing reviewed his later experiences with acoustic tumors showing that the mortality had been reduced to 4 per cent in his last 50 cases. It was later brought out by Eisenhardt,⁶ in looking up the patients in Doctor Cushing's series who had survived five years or longer, that 77 cases of acoustic neuromata fell within this category, and of these, 63 were still living from five to 26 years—a record which has not been approached for this type of operation by any other neurosurgeon. Mere survival, however, does not tell the whole story although in this instance it was an enormous stride ahead in the treatment of these growths. Possibly a better idea as to what could be expected from a radical intracapsular enucleation was reported by Cairns⁷ in reviewing the condition of the patients he had seen on Doctor Cushing's service after an interval of nine years. There were ten cases of acoustic tumor in this series and of this number there were eight survivors. Of these, three were at work, three were severely incapacitated and two had considerable disturbance of gait. Van Wagenen,⁸ in 1934, made a similar follow-up study of a series of Doctor Cushing's cases after an eight-year interval. Of the 11 acoustic tumor patients, seven were living, and of these, four were "in excellent condition and able to go about their usual duties." The other three were up and about although two had been blind before operation and had remained so.

The second great step toward a more permanently satisfactory operation for acoustic neuromata was furnished by Dandy,⁹ who, in 1922, outlined a method for the total extirpation of these tumors, and, in 1925, reported² five

successful total extirpations The mortality for this operation given by Dandy, in 1932,¹⁰ was 20 per cent Recently (1934), Olvecrona¹¹ of Stockholm has likewise advocated total removal of acoustic tumors by Dandy's method, and in 31 cases his mortality was 19.4 per cent

The operative method offered by Dandy, briefly, is as follows He at first employed a bilateral cerebellar exposure, but more recently¹² (1934) he has advocated a unilateral approach After tapping the lateral ventricle and evacuating as much fluid as possible from the cisterna magna, the outer third of the cerebellar hemisphere is excised, giving an excellent exposure of the growth in the cerebellopontile angle This important step in the technic was used for better exposure of these tumors in the majority of his cases by Cushing⁵ since 1928 The capsule of the tumor is now incised and its contents carefully removed with a curet Following this the capsule is grasped with forceps and drawn away from the brain stem, clipping such vessels as may be encountered The tumor is carefully separated from the fifth nerve above and from the ninth, tenth and eleventh nerves below Finally its attachment at the internal auditory meatus is divided, the tumor removed and the meatus cleaned out

The advantages of complete removal contrasted with even a painstaking intracapsular extirpation of acoustic tumors must be obvious The surviving patients in almost every instance are enabled to return to their former activities, presumably without fear of a recurrence of their tumor The chief disadvantage of the complete operation is the facial paralysis on the side of the lesion, but this can be greatly benefited by a spinofacial or hypoglossofacial anastomosis

In favor of the intracapsular method, one can only say that there is almost never any facial palsy and that the initial mortality, up to the present time, has been about half that of the complete operation in such series as have been reported Against these factors, however, are inevitable recurrence, leading either to a further serious operation or to death, and, thus, a far greater eventual mortality than when the tumors are primarily completely removed In addition, the chances of a patient getting back to useful work after the intracapsular operation are not nearly so great as when the tumor is taken out totally

Nevertheless, there may still be instances in which the less hazardous operation, with sparing of the facial nerve, is indicated, although in our own experience total removal of all acoustic tumors previously unoperated upon has been performed without exception during the last four years Patients are always informed about the resulting facial paralysis, and only one has declined for this reason and had the intracapsular operation elsewhere Without all the adjuncts of modern neurosurgery, however, including a highly trained team, adequate suction and a good electrosurgical unit, it is doubtful whether complete extirpation should ever be attempted

Operative Procedure—The operation which we use is similar to the pro-

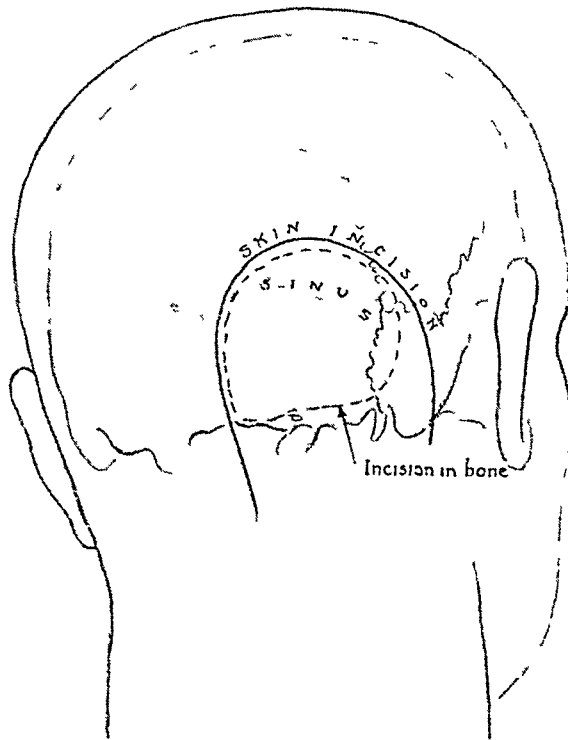


FIG 1—Outline of unilateral skin and muscle flap over the suboccipital region showing its relation to the lateral sinus

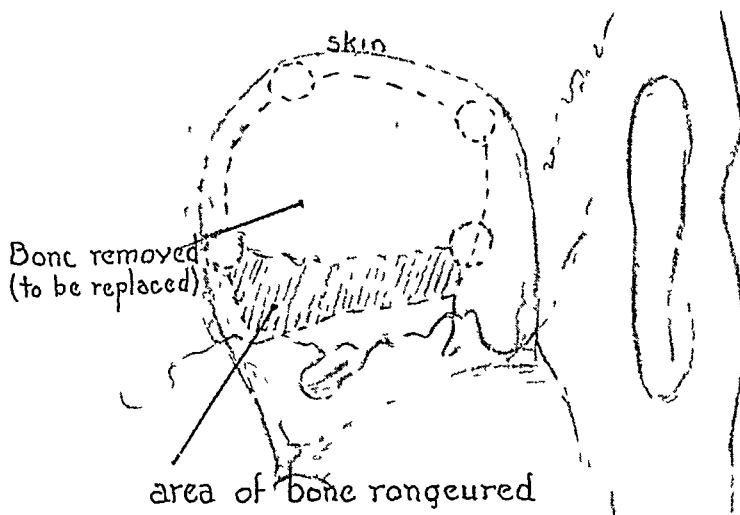


FIG 2—Area of bone removed *en bloc* to be replaced at end of operation. The upper margin of bony opening is well above the lateral sinus. Further bone removed by rongeurs in lower portion of field for full exposure.

cedures described by Dandy and Olivecrona with certain modifications which we believe are important

In the first place, a rather large unilateral skin and muscle flap is turned down over the suboccipital region on the side of the tumor (Fig 1) Following this, a piece of bone is taken out by the use of burr holes connected with the Gigli saw, going well above the lateral sinus (Fig 2) This bone is replaced at the end of the operation Further bone is removed by the rongeur at the lower margin of the area The dura is next opened to the limits of the bony opening, except superiorly

where it is incised up to the edge of sinus This permits exposure directly down the tentorium The outer third of cerebellum is always uncapped, after which the lateral aspect of tumor is fully exposed in the angle From this point our procedure is almost identical with Dandy's The capsule of growth is incised, and its contents evacuated as thoroughly as possible, great care being taken not to get through the capsule medially (Fig 3) Some tumors are highly vascular, and bleeding from the interior has to be controlled by pressure with cotton moistened in saline or sometimes a little Zenker's solution may be used on cotton Likewise the capsules of different tumors vary greatly in their toughness, but most of them can be grasped and drawn gently away from the cerebellum and pons while strips of moist cotton are inserted as the entering vessels are clipped It is usually fairly easy to separate the growth from the lower group of nerves (ninth, tenth and eleventh), but there is almost always a large branch from the vertebral artery at this lower pole and this must be ligated with silver clips (Fig 4)

Separation of the tumor capsule from the fifth nerve is often difficult, due to great adherence, but as a rule it can be accomplished without too great contusion (Fig 5) This is highly important, as the combination of facial paralysis together with facial anesthesia leads frequently to corneal complications When the fifth nerve has been damaged, it is our custom to suture the outer portion of the eyelids to each other, thus giving the cornea almost complete protection

When the tumor has been mobilized at its upper and lower poles, and partial separation from the pons has been accomplished, the tumor's attachment at the internal auditory meatus is divided by cutting and coagulation This permits the final withdrawal of the capsule from the side of pons and medulla, thus completing the enucleation except for that portion of growth within the

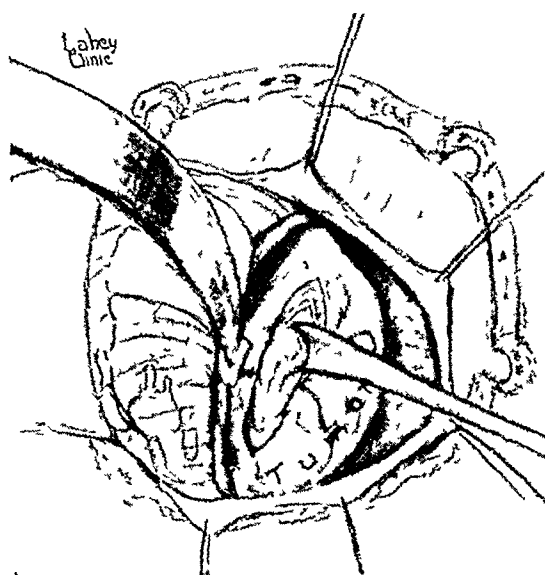


FIG 3—Outer third of cerebellar hemisphere "uncapped" Tumor exposed in the angle Pie liminary excavation with curet

meatus (Figs 4 and 6) This is cuetted out and coagulation applied Often, too, it has been necessary to chip off the bony ridge over the meatus in order to expose it thoroughly and to be sure of getting tumor cells lying far within it

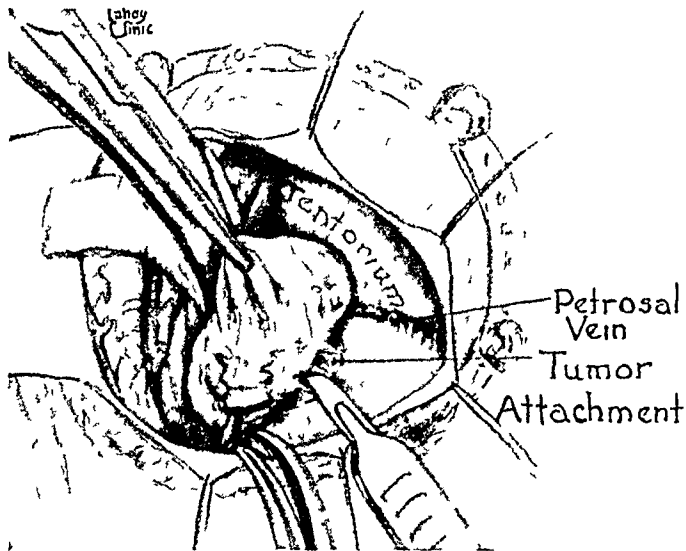


FIG 4—Tumor capsule grasped with forceps and lifted upward Large artery at lower pole ligated with silver clip Tumor attachment at internal auditory meatus divided with knife after coagulation

The bed from which the tumor has been taken should be left completely dry, otherwise postoperative oozing will take place, a clot will form, and reopening of the wound will be necessitated After careful hemostasis the dura

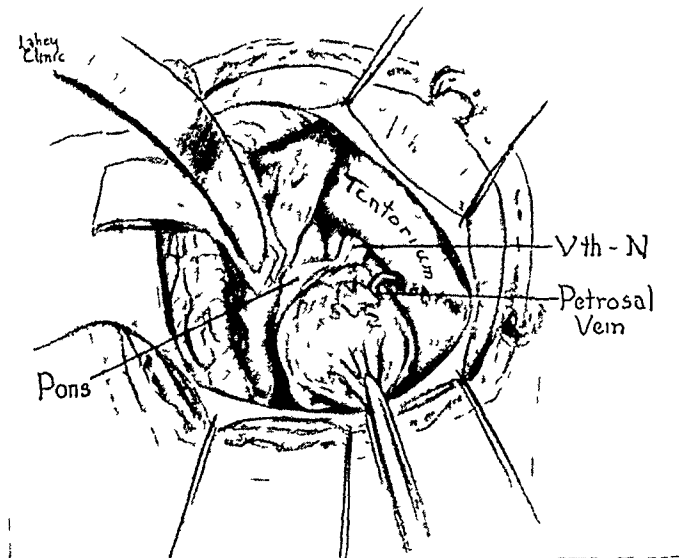


FIG 5—The tumor drawn downward and separated from the trigeminal nerve at its upper pole

is resutured, the upper piece of bone replaced and the skin and muscle flap closed in layers with fine silk without drainage While the convalescence of many of these patients is uneventful they must all be watched carefully, par-

ticularly for difficulty in swallowing and inability to get rid of mucus secretion in the throat. Such secretion should be sucked out promptly by using a fairly small catheter attached to a suction apparatus, passing the catheter either via the nares or the mouth. Nasal feeding is carried out until the patient can swallow well without choking.

Correction of Facial Paralysis—Any time after a two weeks' interval a spinofacial anastomosis is made. In our experience, this is preferable to using the hypoglossal nerve unless the spinal accessory has been injured. Such an

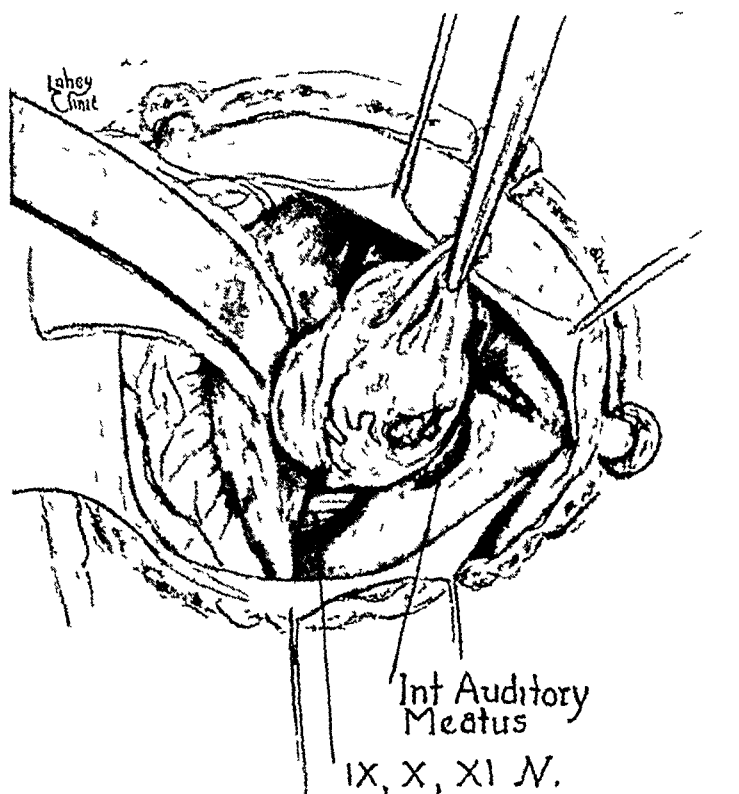


FIG 6—Final mobilization of tumor after its attachment has been divided. The ninth, tenth and eleventh nerves are seen as a group under the tumor's lower pole.

anastomosis gives reasonably good facial function within about a year (Fig 7). In one patient, the facial nerve was preserved at operation, although in this instance it is possible that a few cells may have been left within the meatus (Fig 8). A similar episode was reported by Cairns¹³ in 1931.

Material, Statistics and Results—In the present study there are included all cases of verified acoustic tumors seen since the organization of the Neurosurgical Service at the Lahey Clinic, November 1, 1932 (six and one-half years ago). There have been 35 patients in all, but for obvious reasons they must be divided into two groups, namely, those not having been operated upon previously, 23 in number (Group I), and the recurrent cases, of which there were 12, all of whom had had one or more previous intracapsular partial extirpations (Group II). The reason for this division is because the difficulties and dangers in the complete extirpation of recurrent tumors are infinitely greater than is the case with tumors which are exposed for the first time. In fact, Dandy¹⁰ goes so far as to say that "after one operation has been

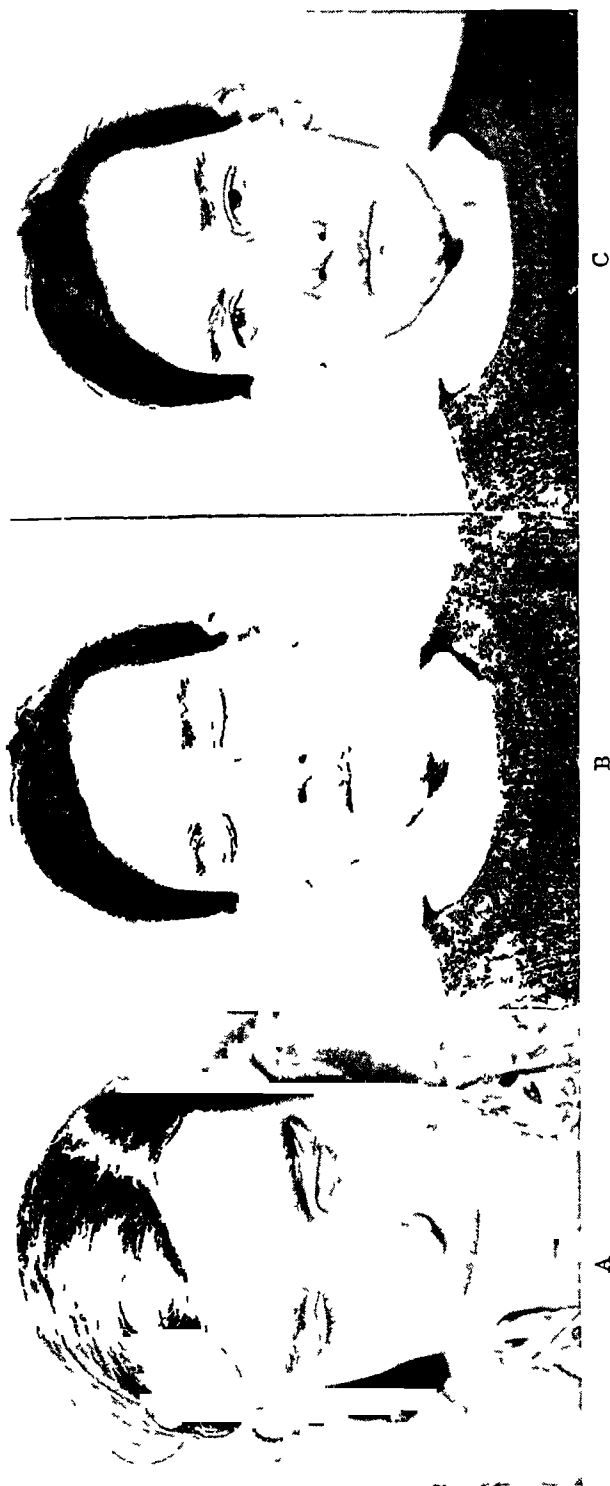


FIG. 7—(A) Patient with left facial paralysis after removal of acoustic tumor (B) The same patient eight months after a spinofacial anastomosis showing ability to close left eye completely (C) The same patient with face in repose after the anastomosis

performed, the adhesions are so great that careful dissection of the tumor at a later date is practically impossible." Therefore, a fair comparison of our series with those of others is possible only when the number of primary and



FIG 8—Patient whose facial nerve was spared at operation (A) Slight left facial weakness three weeks postoperative (B) The same patient two years later

recurrent cases, with their respective data, is known. This may be given in the following summaries:

TABLE I

CASES PREVIOUSLY UNOPERATED UPON

Group I	Cases previously unoperated upon	23
	Intracapsular removal	3
	First stage suboccipital decompression	1
	(No deaths in hospital. All have died subsequently, 1 to 3 years, 3 from recurrence, 1 from intercurrent cause.)	
	Complete removal	19
	Deaths	2
	Mortality	10.5%
	Total operative mortality for Group I	8.7%

Comment—There is little to be said concerning the patients in both groups who had incomplete intracapsular enucleations. There were only six in all, and the survivors, on the whole, did not do as well as had been expected. It was for this reason, doubtless, that we were led into attempting complete extirpations.

The 19 patients in Group I, who had their tumors totally removed, are perhaps of chief interest, since they were operated upon before previous surgical intervention, and, therefore, with a few exceptions, had not suffered severe

brain stem or cranial nerve damage. Two of the patients in this group, unfortunately, were blind before they came for operation, a circumstance which is lamentable in the light of our present knowledge of the diagnosis and treatment of intracranial tumors.

There were two deaths among the 19 patients in this group, one from meningitis which developed 16 days postoperatively, presumably from an opened mastoid cell, and the other from pneumonia in a man who had not only the usual intracranial neuroma but also a large paravertebral extension of his tumor outside the spinal column in the upper cervical region. He was in extremely poor condition before operation.

The 17 surviving patients are all alive from two months to four years since their operations. All but two are either in good or excellent physical condition, able to get about perfectly well by themselves, and, for the most part, to resume their former occupations. This of course does not apply to the two patients who were blind before being operated upon. Three patients have had corneal complications because of damage to the fifth nerve, but none has had to have an eye removed. Several other patients have had a moderate degree of trigeminal hypesthesia, but sensation is sufficient to allow a corneal reflex. Nearly all the group have had spinofacial anastomoses by one of us (J. L. P.), so that their facial paralyses have been greatly benefited (cf. Fig. 7). The amount of ataxia and unsteadiness varies considerably in the different individuals, but tends to be minimal after the lapse of a year.

TABLE II

CASES HAVING BEEN PREVIOUSLY OPERATED UPON

Group II	Recurrent cases	12
	(Patients previously operated upon by us or elsewhere, intracapsular removal having been performed)	
	Further intracapsular removal	3
	Deaths	2
	Mortality	66 6%
	Complete removal	9
	Deaths	3
	Mortality	33 3%
	Total operative mortality for Group II	41 6%

In Group II, there were nine patients whose tumors were entirely extirpated. As intimated previously, the difficulty here was excessive, not only from adhesions to the brain stem but also because of the tremendous extension of the tumor—sometimes far beneath the pons to the opposite side, entirely covering the basilar artery and likewise extending upward into the incisura and downward into the foramen magnum. Three of the nine patients died—all from pulmonary complications due to difficulties in swallowing. The six living patients are all in surprisingly good condition considering their previous disability. Three have been able to resume their former occupations, and the other three are able to do work about the house although one has been nearly blind since the time of his first operation.

SUMMARY

The operative and end-results in a series of 35 patients with verified acoustic tumors are presented. Certain features of the operative technic for the total removal of these neuromata are given in detail. Since, in our hands, intracapsular removal of the tumors has been unsatisfactory and the eventual mortality extremely high, complete extirpation is now carried out on all cases, whether primary or recurrent. The operative as well as the total mortality for complete removal of tumors previously unoperated upon is 10.5 per cent. When this procedure has been carried out on recurrent tumors the mortality is 33.3 per cent. The combined mortality for both primary and recurrent tumors totally extirpated is 17.8 per cent.

REFERENCES

- ¹ Cushing, H. Tumors of the Nervus Acusticus, and the Syndrome of the Cerebello-pontile Angle. Philadelphia, W. B. Saunders Co., 1917.
- ² Dandy, W. E. An Operation for the Total Removal of Cerebellopontile (Acoustic) Tumors. Surg, Gynec and Obstet, 41, 129, 1925.
- ³ Cruveilhier, J. Anatomie pathologique du corps humain. Paris, 1835-1842.
- ⁴ Tooth, H. The Treatment of Tumours of the Brain and the Indications for Operations. Trans Internat Cong Med, Sec VII, Pt I, 203 London, 1913.
- ⁵ Cushing, H. Intracranial Tumors. Springfield, Ill, C. C. Thomas, 1932.
- ⁶ Eisenhardt, L. Long Postoperative Survivals in Cases of Intracranial Tumor. Proc Asso for Res in Nerv and Ment Dis, 16, 390, 1935.
- ⁷ Cairns, H. The Ultimate Results of Operations for Intracranial Tumors. Yale Jour Biol and Med, 8, 421, 1936.
- ⁸ Van Wagenen, W. P. Verified Brain Tumors. End-Results of One Hundred and Forty-nine Cases Eight Years After Operation. J A M A, 102, 1454, 1934.
- ⁹ Dandy, W. E. An Operation for the Total Extirpation of Tumors in the Cerebello-pontine Angle. A Preliminary Report. Johns Hopkins Hosp Bull, 33, 344, 1922.
- ¹⁰ Dandy, W. E. Practice of Surgery (Dean Lewis), XII. Hagerstown, Md, W. F. Prior Co., 1932.
- ¹¹ Olivecrona, H. Technik und Ergebnisse der Radikaloperation bei Acousticstumoren. Arch f klin Chir, Kongresband 180, 1934. (Verlag von Julius Springer, Berlin).
- ¹² Dandy, W. E. Removal of Cerebellopontile (Acoustic) Tumors Through a Unilateral Approach. Arch Surg, 29, 337, 1934.
- ¹³ Cairns, H. On Conserving the Facial Nerve During Removal of Tumors of the Cerebellopontine Angle. Proc Roy Soc Med, 25, 7, Sec Neurol, London, 1931.

DISCUSSION —DR MAX M. PEET (Ann Arbor, Mich.) We have used a unilateral approach for acoustic tumors during the last ten or 12 years, and it certainly has many advantages. We have also been performing as complete as intracapsular excision as possible and then pulling the capsule out—in other words, complete extirpation of the tumor. We felt that this was necessary for the same reason that Doctor Horrax does. Some patients had remarkably rapid recurrence. One such patient Doctor Horrax happened to see me operate upon. I had taken out the whole tumor, including all the capsule except that portion extending into the internal auditory meatus. I wanted to save the facial nerve, and I had succeeded in saving it up to that point, and so we left a small amount of tumor inside the internal auditory meatus. Within six months his symptoms had all returned, and at operation I found the tumor just as large as the original one. In fact, the gross appearance did not seem

to be much different. At the second operation I took out the whole tumor and then thoroughly cauterized, using the Bovie unit, everything within the internal auditory meatus. I think we are justified in producing a facial paralysis in all these individuals. It can be corrected by a spinofacial anastomosis. The latter preserves the tone of the face and the patients can smile voluntarily. I admit they do not smile involuntarily. If they want to make a good appearance, they have to think about smiling, but that is infinitely better than having a recurrence, as some patients do in a comparatively short time.

I think the actual mortality for complete excision of acoustic tumors by the technic Doctor Horrax has shown, is no greater than the partial operation which has been performed so many times before, and the final results, so far as the patient is concerned, are infinitely better.

DR. FREDERICK L. REICHERT (San Francisco): The discontinuance of the whose exposure of the cerebellum and the use of the unilateral approach with a deliberate resection of the outer part of the cerebellar lobe has made a marked improvement in the operative removal of the acoustic tumors.

We have tried to save the facial nerve, which is a much tougher nerve than the eighth, and by carefully dissecting the capsule down to the seventh nerve and then coagulating it, we have been able, in the last few cases, to preserve the facial nerve. I think that is a procedure that might be tried in many of the cases.

DR. GILBERT HORRAX (closing): There was one thing which I neglected to mention, and that concerned the internal auditory meatus. We did save the patient's facial nerve in one instance, but in my experience, the tumors always extend well into the internal auditory meatus to quite a considerable depth and, therefore, if you are going to be sure of getting every cell out, you must deal with it in some way, and what I should have said was that we always curet the meatus, and not only that, but it has been found necessary, very usually, to either chip off the bony ridge over the meatus so that you can get at it better, or make some bony openings there with a small drill and take it off that way, lest you should break into the mastoid cells by chipping it off. Then we not only curet out the meatus, but also coagulate as far in as possible with some suitable instrument.

Now, it is true, as Doctor Reichert says, and as we have done once and as Dr. Hugh Cairns, of London, has done once, as doubtless others have, that we can save the facial nerve, but I am very sure in so doing we do leave some cells.

It is obvious that not all of these tumors are going to recur as rapidly as the one Doctor Peet has mentioned, because some of them have gone on for many years. On the other hand, I feel we are leaving a loophole for recurrence if we do spare the facial nerve, although one would always like to, so it is our custom, almost invariably, to curet out the meatus and cauterize it with the electrosurgical outfit so that we can be sure of not leaving any cells to recur.

INTRACRANIAL ARTERIOVENOUS ANEURYSMS*

ALBERT O SINGLETON, M D

GALVESTON, TEX

It is with an apology that I impose upon this Society a paper upon a subject which has been studied and analyzed so many times by those who have had more extensive and much more expert knowledge than I. Still, there is an unexplainable fascination about vascular disorders and they offer a real challenge, for the anatomy and circulation of the blood have not completely lost their mystery, though Harvey has been dead for nearly 300 years. The addition of four cases to the long list of intracranial arteriovenous aneurysms already reported is a small justification for the paper, and yet each one shows some points of interest, either in anatomy or in its response to treatment.

Because the larger arteries and veins within the skull do not parallel one another, fistulae, other than the congenital angioma where direct arteriovenous communications occur without capillaries intervening, are rare except for the carotid-cavernous sinus type, which may be congenital or more often traumatic in etiology. But, as has been frequently noted, because of the unusual anatomic situation of the carotid artery within the cavernous sinus before it reaches the brain, such fistulae are relatively common. The cirroid intracranial aneurysms, though less frequent, are often confused with the carotid-cavernous types. Two of the cases here reported are of this type and are of a serious nature. The problem of dealing with them is no less interesting than the two carotid-cavernous cases.

CASE REPORTS

Case 1—U H No 24892 J W T, white, male, age seven, entered the John Sealy Hospital, May 17, 1928, giving the following history. Since birth the right side of the face had been of a darker color than the left and had appeared dusky and flushed at all times. The condition had grown steadily worse during the past few years.

Physical Examination revealed a well-nourished child, not acutely ill. The whole right side of the face, scalp, and upper part of the neck was dark and cyanotic in appearance. The superficial veins were engorged and could be seen pulsating. The condition was not that of a cavernous hemangioma since only the normal number of veins were present, although they were greatly engorged over the entire half of the face and head. The right eye showed a moderate proptosis with congestion of the conjunctiva. On auscultation, a loud bruit could be heard over the entire right side of the head, face, and neck. There was a fairly sharp line of demarcation between the two sides of the face. Pulse ranged from 110 to 120 at rest. The eye examination showed the retinal vessels congested, but vision was apparently not defective.

We considered this a congenital cirroid aneurysm after exploring the carotids and finding no fistula between the carotids and jugular vein, but the location of the cirroid aneurysm was never definite, and even now we are reluctant to predict its location. Still, there is a possibility that there may have been a carotid-cavernous aneurysm as well. The treatment was the same as if it had been such an aneurysm.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

Operation—May 17, 1928 The common, internal and external carotids were exposed on the right side. No fistula was found. The common carotid was occluded with a Halsted aluminum band. No cerebral symptoms developed, and following the operation there was much less engorgement of the veins of the face and eye, the murmur persisted, though it was much less pronounced.

On July 28, 1928, the patient was again admitted to the hospital. There was only slight improvement since the previous admission, and, according to the records, there was a very marked to-and-fro, swishing murmur audible over the right side of the face and head, much less marked on the left side. Vision in the right eye was markedly diminished, and the eye was prominent. It was thought that collateral circulation through the branches of the external carotid had restored the circulation.

Second Operation—July 29, 1928 The right external carotid was exposed and ligated. It showed only slight bleeding when cut. The facial, lingual, occipital, and other

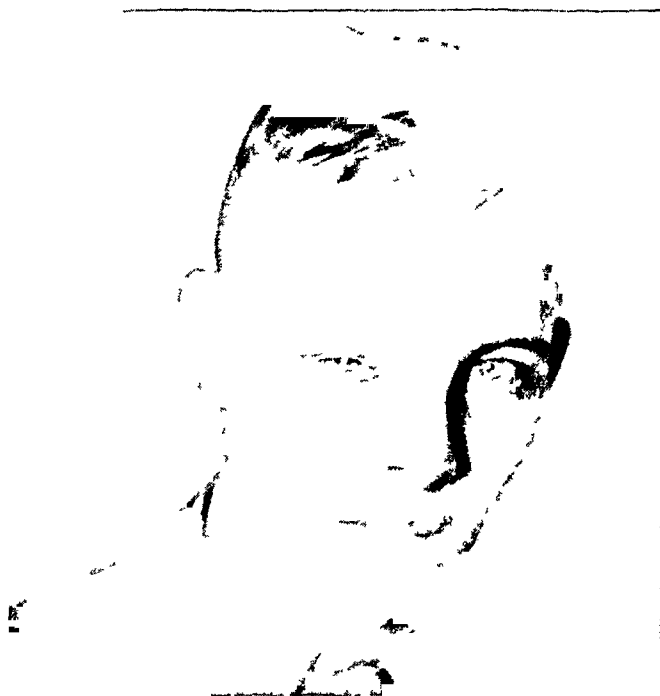


FIG 1—Case 1 Patient ten years after carotid occlusion for cirroid intracranial aneurysm resulting in hemiplegia

branches were separately ligated. Following this operation the right side of the face was much less congested, and the murmur was much less pronounced, but to our surprise it now appeared louder on the left side of the face and neck. This change was difficult to explain. The patient went home on the fifth day, and on the ninth day after operation his mother noticed that his left hand, arm, and leg were partially paralyzed.

The patient was not seen again until March 1, 1939 (ten years later), at which time we found him a boy of 18 years, weighing 160 pounds. He was lame with the gait of the average long-standing hemiplegic. The left leg was smaller than the right and quite spastic, with exaggerated reflexes. The left arm was small, spastic, and underdeveloped. The face was not involved in the paralysis, but the right side of the face and head was much larger than the left (Fig 1) and was of a dusky color due to the great engorgement of all the superficial veins. As on the first admission, the line of demarcation between the two sides of the face was sharply defined. The right eye was prominent, and the conjunctival veins were engorged. A systolic murmur was present over the head, face, and eyes, still much louder on the left, or unaffected side. The heart sounds were regular with a rate of 110 to 120. Compression of the right jugular increased the con-

gestion Compression of the left carotid did not effect the murmur Palpation on the right side of the skull revealed irregularities in the bone beneath the varicose veins Roentgenograms showed extensive calcification over the cortex of the brain on the right side with grooving of the skull in many pieces from the dilated scalp veins Sight in the right eye was almost lost Fingers could be counted by this eye, but nothing more Vision in the left eye was corrected to good sight with glasses The mentality of the boy was slightly below normal

Roentgenologic Study—"The teleroentgenogram shows quite an increase in the cardiac shadow, the percentage of increase at the apex being 16.3 Studies of the skull show an unusual type of calcification over the right half of the cranium extending from the frontal area posteriorly to the occipitoparietal region The calcification appears to be within the skull, and is apparently in the meninges or the cortical area of the brain Throughout this area one can see canalizations which give the impression of vascular channels, suggesting that this calcification might be an extensive hemangioma of the cranium in the right parietal area There is marked thinning of the right temporal region There is an irregular increase in the thickness of the skull Irregular defects in the frontal area due to dilatation in the emissary channels There is extreme dilatation of the diploic channels, especially in the right side"

Discussion of Case 1—There is some question as to the correctness of our assumption that there was a carotid-cavernous sinus fistula in addition to the cavernous angioma, but because of the eye symptoms we could not ignore this possible conclusion

Nine days following the internal carotid occlusion, this patient developed a hemiplegia Whether this was due to cerebral anemia following ligation or the extension of a thrombosis to the circle of Willis, or due to an embolus dislodged from an old thrombosis resulting from the carotid ligation, we cannot say It seems more logical to attribute the paralysis to the cause last mentioned This complication might indicate that occlusion of the carotid in the young is not without danger, though not necessarily so Another interesting observation was the shifting of the murmur to the left side of the head and neck following the occlusion of the carotids on the right side

The results of the embolus were very deplorable The cerebral accident was more distressing than the original affliction The carotid occlusions had improved the condition only temporarily, and the location of the fistulae was still obscure We surmised that they were intracranial and multiple In the beginning we felt that there was an opening between the internal carotid and the jugular at the base of the skull Though there was a great deal of back pressure in the ophthalmic veins of the right side, we could not be sure it was a carotid-cavernous fistula At the present time the patient's parents will not agree to further treatment

Case 2—Hosp No 57334 Mrs R, white, female, age 53, entered the hospital, January 21, 1938, complaining of a roaring in her head, headaches associated with vomiting, and a staggering gait The symptoms had begun two years before, and during the past six months they had grown much worse, with the development of an ataxic gait Three months previously, the patient had an unconscious spell and was in bed several weeks with dizziness Neurologic and physical examination showed the patient to be a slight woman, undernourished and ill The pupils were equal and reacted to light The disks appeared normal Ocular muscles were intact with some lateral nystagmus There

was no facial weakness, but there was a marked cerebellar ataxia. Equilibrium was better on the right foot than on the left. There was ataxia on heel-to-knee test on both sides, more marked on the left. Motor power and muscle status were normal. There were no pathologic reflexes. There was only slight bone conduction of the left ear. The left fifth and eighth nerves were definitely involved, suggesting a posterior fossa lesion.

There was a visible pulsation of the vessels below the left ear and over the left mastoid area, and a palpable thrill was found in this region. A loud systolic murmur was heard over the entire head, loudest over the left mastoid region and less pronounced on the right. Compression of the right carotids did not influence the murmur, nor did compression of the left common carotid. But compression of the carotid on the left side at the bifurcation stopped the noise completely. The veins of the head were only slightly congested. Roentgenogram of the skull was negative. *Diagnosis* Intracranial arterio-venous aneurysm of the cirroid type.

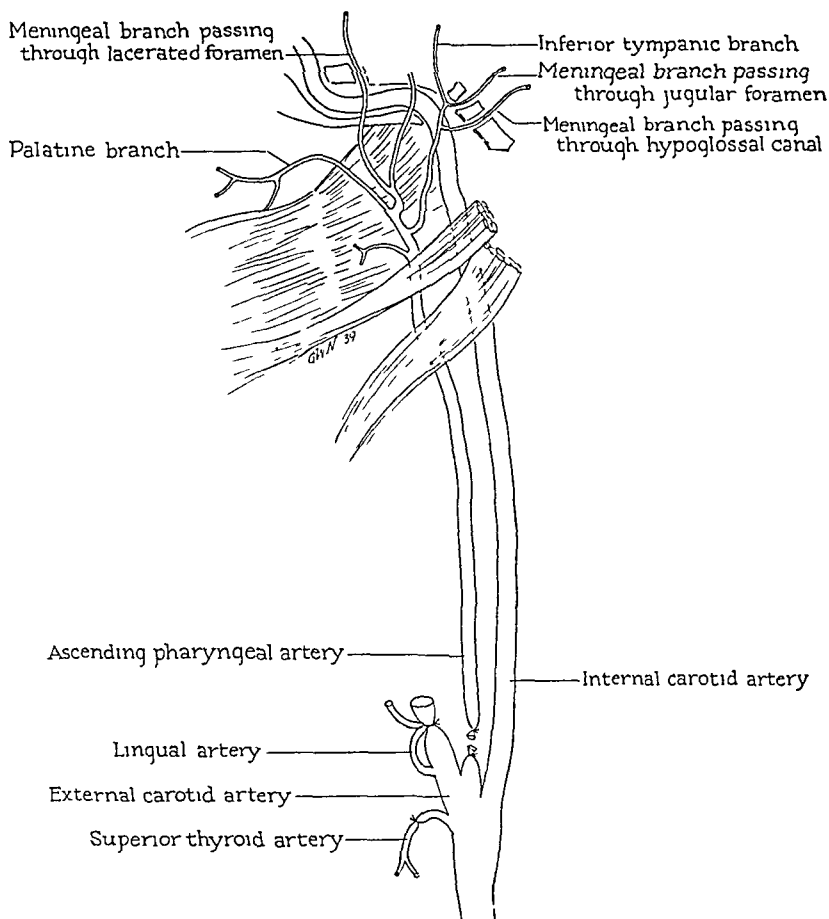


FIG 2—Case 2 Greatly enlarged ascending pharyngeal artery supplying chief circulation to intracranial cirroid aneurysm

Operation—February 1, 1938 The left carotid vessels were exposed under local anesthesia. Arising from the fork of the common carotid was an abnormally large vessel, evidently the ascending pharyngeal, which is ordinarily very small but here was half as large as the internal or external carotid (Fig 2). It was thin-walled and more purplish in color than the large arteries. Compression of the common carotid did not affect the murmur, nor did compression of the internal and external separately. Occlusion of the ascending pharyngeal stopped the murmur. This vessel was cut between ligatures, and the external carotid was also ligated. Convalescence was uninterrupted, and the patient remained in bed for ten days. She was much better in every way, the

roaring in the head had gone, headache and vomiting and ataxia gait were greatly improved. She left the hospital, February 12, 1938.

The patient entered the hospital again on March 28, 1938. She was in good general condition, but there was nerve deafness in the left ear as before. There was no ataxia, and the patient heard the murmur only slightly, but the palpable pulsation had returned over the left mastoid area though it was less pronounced than previously. A bruit was heard over this area, more limited than before. The left superficial temporal artery was not palpable.

Second Operation—March 29, 1938. A curved incision was made down to the skull over the mastoid region, surrounding the vascular area previously described, and the flap was turned up with all branches of the great auricular and occipital arteries severed and tied. The large emissary mastoid vein was ligated as it entered the skull. The result was a cessation of the murmur as well as the pulsation.

A follow-up in February, 1939, reported that the patient was comfortable, free from all symptoms except the left ear deafness and the presence of a faint bruit.

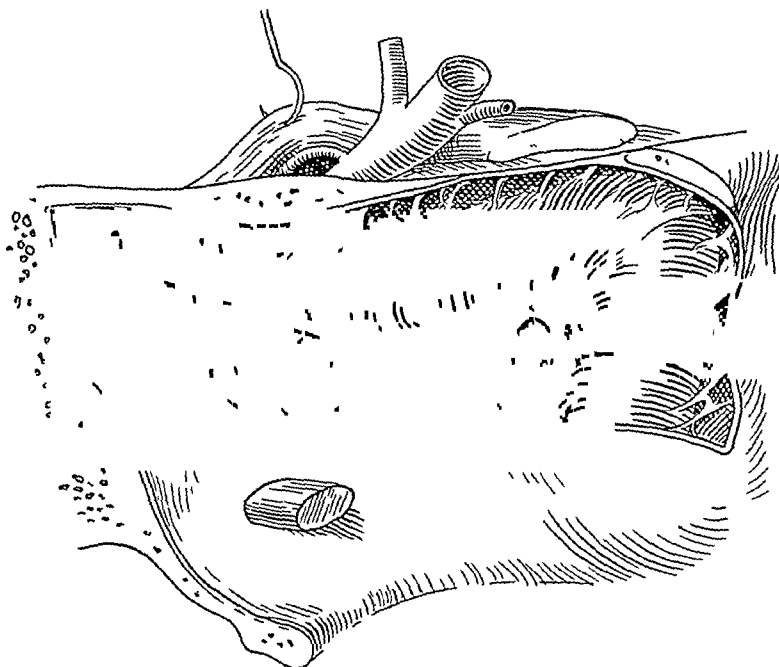


FIG 3—Internal carotid after passing through cavernous sinus (after Jackson)

Discussion of Case 2—This case is of anatomic interest because of the part played by the ascending pharyngeal artery, which has assumed enormous proportions, though normally it is very small and insignificant. This artery passes upward, supplying branches to the pharyngeal-tympanic tube and palate, and its *inferior tympanic* branch accompanies the tympanic branch of the glossopharyngeal nerve to the tympanic cavity. It also gives off the posterior meningeal, branches of which enter the skull through the foramen lacerum, jugular foramen, and anterior condylar canal. The ligation of the ascending pharyngeal artery decreased the activity of the aneurysm. Though the murmur and thrill disappeared for some time, improvement was permanent only after destroying externally the communicating circulation through the cranial vessels over the mastoid and occipital regions, which was chiefly through the large emissary mastoid vein into the cranium.

Carotid-cavernous aneurysms have been given a most thorough study and

extensive discussion in medical literature, and still they have their hidden, unexplained problems. Locke collected from the literature 588 cases reported prior to 1923. Doiran and Loudenslager reviewed 275 cases occurring between 1908 and 1934. These represent a small number of the cases actually occurring. The contributions of H. Sattler, deSchweinitz, C. H. Sattler, Matas, Locke, and more recently Dandy, should be carefully studied and restudied before one attempts to treat such an aneurysm. We offer very little new upon the subject, but submit the reports of two cases, some features of which are of interest as an anatomic study, as well as the results of the treatments employed.

Case 3—U. H. No. 26069. M. R., Negro, female, age 39, entered the John Sealy Hospital, September 27, 1928. She was a well-nourished Negress, not acutely ill. She stated that for the past two months the right eye had been swelling at night and subsiding in the morning when she got up. She had had pain in the eye in addition to the swelling. One week following an attack of influenza she was awakened at night by a feeling as if "something turned loose inside her head and there was a noise in her right ear like a train puffing and roaring." It seemed as if the sound came from under the pillow. From the time of onset this noise annoyed the patient constantly. It was somewhat worse at night.



FIG. 4.—Case 3. Ten years after cure of pulsating exophthalmos by unilateral ligation of common and internal carotids.

Physical Examination revealed that the pupils were unequal (right 4 mm., left 3.5 mm.) but they reacted to light and accommodation. There was some puffiness of the upper lid, evidently an engorged vein. Congested veins stood out in the right sclera, and there was slight exophthalmos of the right eye. There was some congestion of the conjunctiva. Both eyes were sensitive to light, and dark glasses were worn. Movements of the eyes were normal except for a slight external deviation of the right eye to three degrees. The iris on the right side was congested, and there were enlarged veins on examination of the fundus. The veins on the right side of the neck were engorged and visibly pulsating. A loud systolic murmur was heard all over the right side of the neck and head, being most marked over the temporal region and the right eye. Firm pressure on the right

common carotid stopped the bruit but caused pain. The pulse was regular, 100 per minute, blood pressure 150/90. A harsh systolic murmur was pronounced over the aortic area and was transmitted to the neck. There was no evidence of an aortic aneurysm. Roentgenograms of the skull and chest were negative. Blood Wassermann was negative. *Diagnosis*: Carotid-cavernous aneurysm of the right side.

Operation—October 15, 1928. Under local anesthesia an aluminum band was applied to the common carotid of the right side, and the artery was completely occluded. The patient said the noise disappeared. The venous congestion in the eye immediately improved, but after a few weeks the noise, murmur, and eye congestion reappeared, though

they were less marked than before operation. The patient was admitted to the hospital two months later.

Second Operation—January 30, 1929. Local anesthesia. Much scar tissue was found about the right common carotid at its bifurcation, resulting from the previous operation. The metal clip was found in the scar. It had cut through the artery and become encysted. Following ligation of the internal and external carotids separately with chromic catgut, the noise ceased.

The patient was examined again in February, 1939, ten years later. There had been no return of symptoms. The eyes were normal in appearance (Fig 4) and vision was good except for changes due to age. The aortic valve systolic murmur was still present. Blood pressure 200/100. An E K G was normal, and Wassermann tests were again negative. The patient had enjoyed good health and had been regularly employed as a cook for the past ten years.

Discussion of Case 3—That this was a carotid-cavernous aneurysm can hardly be questioned even though no history of traumatism preceded its development. This patient had an aortic valve murmur, and though the blood Wassermann was negative, syphilitic arteriovascular disease is so common among the Negro race that we may theorize that this instance of perforation of the carotid artery into the cavernous sinus was the result of syphilitic arteritis. The patient was cured, as are 40 per cent of such cases, by unilateral obstruction of the common and internal carotid artery.

Case 4—Hosp. No. 61173. A. L., white, female, age 32, entered the John Sealy Hospital in December, 1938. She had always enjoyed good health until November, 1930, when she was in an automobile accident and was unconscious for 12 hours, during which period there was bleeding from both ears and from the nose. When she regained consciousness, she noticed a swishing noise in her head which persisted without remission. After four months the right eye began to protrude and pulsate.

On April 22, 1932, Dr. R. B. Alexander of Waco, Texas, ligated the right common carotid artery with two catgut ligatures, and the artery was cut between. The pulsation apparently disappeared, but by October the condition was about the same as before the operation. On October 23, 1932, the right internal and external carotids were ligated and severed. Recession of symptoms was for a short time only. At the present time the prominence of the eye and the dilatation of the veins over the forehead reappeared. For the past two years the vision of the right eye had been failing, and now the patient was unable to read with it. The vision of the left eye was good.

Pulse 95, regular and of good volume. Blood pressure 112/70. There was a marked protrusion of the right eye, the exophthalmometer reading being 27 Mm (Fig 5). The veins in the sclera, above the eyeball, below the eyeball, and over the forehead were all dilated and visibly pulsating. A systolic bruit could be heard over the entire head but was loudest over the right eye and the right side of the head. With compression of the left carotids, which the patient tolerated, the bruit decreased. The eyes showed weakness of the lateral muscles. Pupils reacted to light and convergence. The right fundus had a normal disk, but the veins were tortuous. The same condition was present in the left fundus to a less marked degree. Cranial nerves were normal.

Since the carotids on the right side had already been occluded in the neck, intracranial occlusion of the right internal carotid was decided upon.

Operation—January 20, 1939. An osteoplastic flap was turned down over the right frontal region (hypophyseal approach). A large amount of subdural fluid escaped when the dura was incised, and a quantity of subarachnoid fluid also escaped when the very tough arachnoid was incised. This escaping fluid, which seemed excessive in amount, left an abundance of room. Upon elevating the frontal lobe, the internal carotid artery

became quite accessible. It was smaller than the optic nerve alongside it and was purplish in color and not visibly pulsating. A large-sized silver clip was placed astride it and forced together with apparently little pressure within the vessel.

The patient showed no undue disturbance from the operation. The right eye seemed less prominent, and the dilatation of the veins was less marked. The bruit could not be heard anywhere over the head. The right pupil was dilated. Within two weeks the pulsation became faintly perceptible in the right eye. The veins grew more prominent, and the bruit could be heard over the same areas as previously, though not as distinctly. The patient could hear the noise faintly in her right ear.

Following the intracranial ligation, theoretically the blood passing through the fistula must have been backflow through the ophthalmic artery from anastomosis with branches



FIG 5—Case 4. Pulsating exophthalmos right eye six years after right carotids were occluded.



FIG 6—Case 4. Prominent ophthalmic veins present after intracranial occlusion of internal carotid and occlusion of opposite external carotid.

of the external carotid vessel on the left side. It was decided to ligate the left external carotid, and this was done under local anesthesia, February 3, 1939. The bruit was lost as soon as the artery was occluded. The pulsation of the eye ceased, and the dilated veins receded (Fig 6).

Three days later the murmur could be heard with the stethoscope over the left eye, the left side of the head, and down the left side of the neck, although the patient could no longer hear a bruit. No sound was heard over the right eye or the right side of the head.

By March 1, 1939, the murmur was still absent over the right eye but was pronounced on the left side. The orbital veins were filled with blood under a fair degree of pressure. It was decided to inject the ophthalmic veins, and 4 cc of 50 per cent glucose were injected. At the same time an effort was made by pressure to prevent the blood from escaping over the forehead and across the nose. When the needle was introduced into the vein, bright red arterial blood was aspirated. The patient experienced no discomfort, and there was no sign of any sclerosing or clotting following the glucose injection.

Ten days later, an injection of 1 cc of sodium morrhuate was made in the same way. The patient experienced severe pain for 15 minutes or more. Within 24 hours there was a marked reaction, the eye being engorged with blood with a small subcleral hemorrhage and much swelling. The inflammation spread over the forehead, and the eye

condition appeared alarming, but after four or five days the reaction subsided (Fig 7), and thrombosis was evident in the peripheral branches of the ophthalmic veins about the eye and over the forehead. Two months later the eye had receded markedly, vision had improved, and the orbital veins were not visible (Fig 8). The murmur was still faintly audible over the eye, face and neck of the sound side but not on the affected side. The patient was quite happy about the result.

Discussion of Case 4—This case is of interest in that it represents practically all standard procedures generally used for treated carotid-cavernous aneurysms, including the ligation of the carotid artery within the skull as well as the injection of the ophthalmic vein with a sclerosing solution. The



FIG 7—Case 4. A few days after injection of ophthalmic veins with sodium morrhuate. Marked inflammatory reaction.

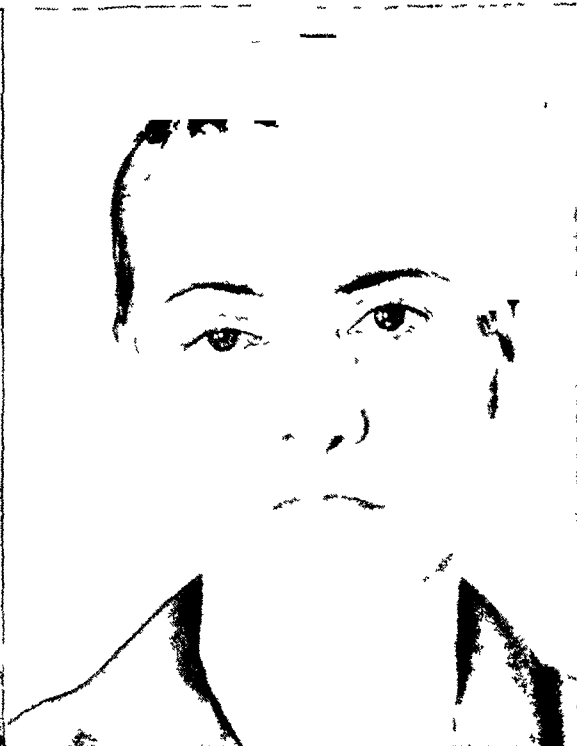


FIG 8—Case 4. Three months after injection. Thrombosis effectual.

obstruction of the common, internal, and external carotid arteries on the affected side failed to influence the symptoms except for a short time. The ligation of the internal carotid within the skull resulted in a marked remission of symptoms. The bruit and pulsation of the ophthalmic vein and the eye ceased for several days but returned in a lesser degree. There was some recession of the eye.

Occlusion of the carotid within the skull, for pulsating exophthalmos, was first performed by Zeller, in 1911, according to Dandy, but due to an accident the patient died of hemorrhage. Hamby and Gardner (1933) ligated the artery intracranially with a silk ligature, as did Zeller. Improvement, but not complete cure, resulted immediately in this case. Dandy, in April, 1934, used a silver clip to occlude the artery intracranially and operated upon a second case in July of the same year. In both instances marked improvement resulted, and in one case there was a cure without further

treatment In the other case, obstruction of the branches of the corresponding external carotid and later a dissection of the ophthalmic veins of the same side were necessary before a complete cure was effected

When one examines the anatomy of the internal carotid artery, it seems quite logical to ligate it inside the skull following ligation in the neck It may readily be seen that the only circulation left then to feed the fistula is through the ophthalmic artery with a reversal of the direction of the flow of blood It is true that there are other very small vessels leaving the internal

carotid in this segment, the carotid-tympanic, hypophyseal, and meningeal branches, but they are very small Still one cannot ignore the compensating enlargement possible in even small arteries when circulatory demands are put upon them Theoretically, it is quite surprising that the sinus should persist as it did in our case and one of Dandy's Though complete cure may not result, great improvement must follow the intracranial ligation if the extracranial ligation precedes it

We wish to confirm the statement of Dandy to the effect that the approach to the carotid intracranially and the application of a clip are comparatively easy procedures and should be accomplished with little danger of a serious accident occurring

Because the sinus persisted after the intracranial ligation, it was evident that the ophthalmic artery was receiving blood from its peripheral anastomosis and likely from the internal maxillary and facial branches from the opposite external carotid (Fig 9)

FIG 9—Rich anastomosis between the ophthalmic and the internal maxillary and facial branches from both sides (after Jameson)

This influenced us to ligate the left external carotid (Our experience in ligation of the external carotid for nosebleed and tonsil hemorrhage has shown on several occasions that occlusion of one vessel alone has little influence on the bleeding, but ligation of the second vessel is quite effective, and sufficient blood is still available for the tissues supplied by the vessels) The ligation of the opposite external carotid and its branches resulted in the complete disappearance of the pulsation from the right eye, the prominent veins decreased, and further recession of the eye resulted The noise to the patient completely disappeared By the stethoscope, the bruit disappeared from the right side of the head and eye but appeared distinctly over the opposite eye and the left side of the head and neck This shifting of the murmur as in Case 1 was quite puzzling The communicating veins between the two cavernous sinuses are quite small normally, but due to the long increased pressure within the sinuses they would have become greatly enlarged Cases are reported by Sattler and

Dandy where the opposite eye became involved following occlusion of the ophthalmic vein on the affected side, which must have been due to the passage of blood through the communicating veins to the other sinus. In this instance, there was not an occlusion of the ophthalmic vein on the affected

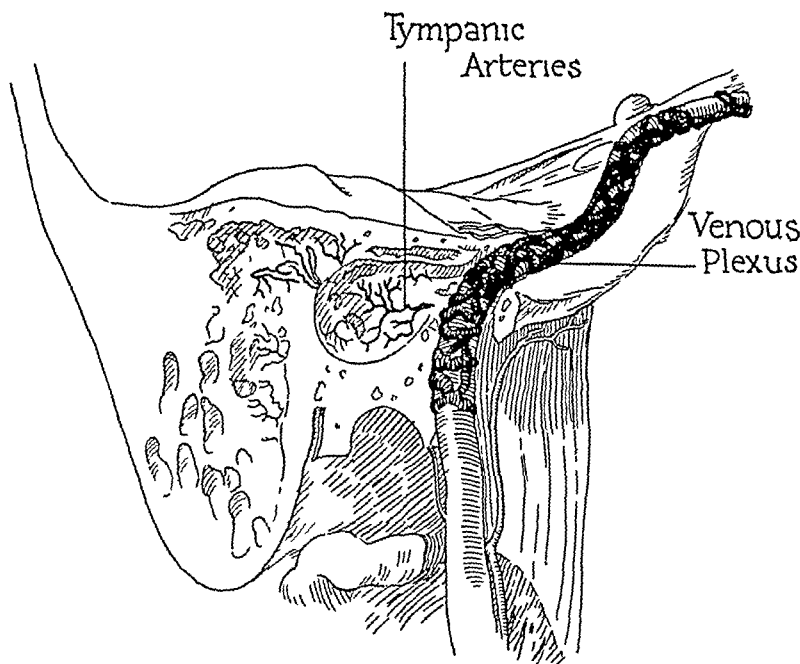


FIG 10—Small branches other than the ophthalmic come off the internal carotid (after Spalteholz)

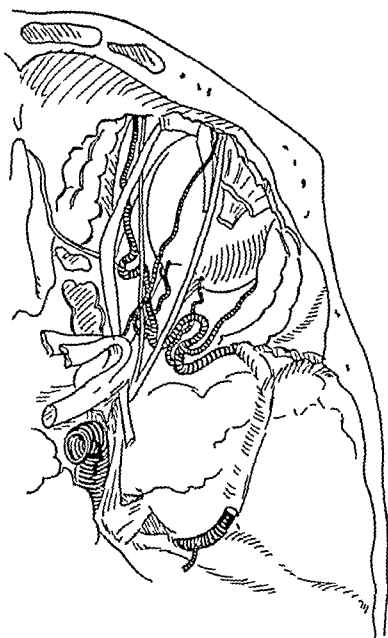


FIG 11—Ophthalmic artery originating entirely from the middle meningeal (after Adachi)

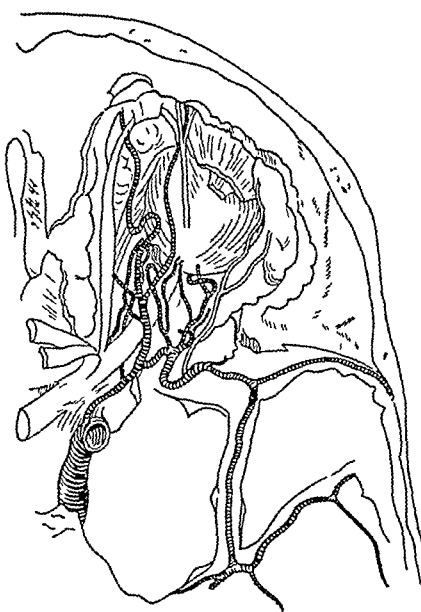


FIG 12—Abnormal anastomosis between middle meningeal and ophthalmic arteries (after Adachi)

side following the ligation of the opposite external carotid. On the other hand, the obstruction of the remaining external carotid greatly lessened the blood flow and pressure in the veins of that side of the face and encouraged the blood to pass through the communicating veins to the other cavernous sinus and into the other ophthalmic vein.

This is a weak explanation of the shifting of the murmur to the unaffected side. Dr C T Stone, a cardiologist of the University of Texas, suggests that this was a new murmur caused by eddies in the current of blood through the remaining internal carotid. Dr George Hermann, also a cardiologist, considers that "the transfer of the murmur to the left side is a part of the compensatory mechanism, which consists in dilatation of the proximal or common carotid artery, even extending as far back as the aorta, and the murmur may be due to the dilatation." These explanations of the shifting of the murmur to the opposite side of the head in Cases 1 and 4 are still not satisfactory. It is true that bilateral fistulae do occur, as reported by deSchwenty, but since there was no evidence of symptoms in the opposite eye previously, we doubt that the murmur was due to another fistula here.

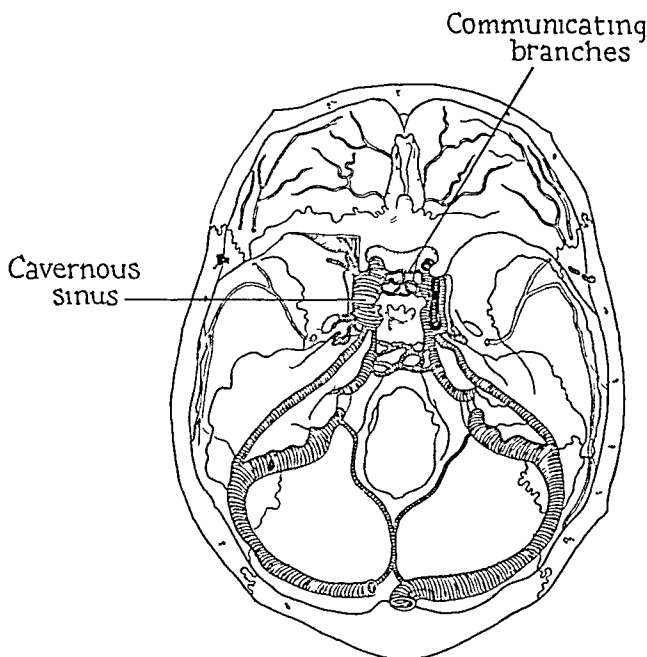


FIG 13—Communicating branches between cavernous sinuses
(after Jameson)

Prognosis in Carotid-Cavernous Aneurysms—The untreated cases may result in (1) Death from hemorrhage in the traumatic cases at the time of injury or later. Nine deaths from hemorrhage from the nose were reported by Sattler, or 3 per cent of all aneurysms collected. (2) Damage to vision and loss of the eye is a common complication, not more than 20 per cent retain good vision, according to deSchweinitz. Nolan reports complete loss of sight in one eye in one untreated case, and in another, not only the sight in one eye was lost but almost complete blindness resulted in the other. If not complete loss of vision, there is often loss of accommodation with deviation of the eye, resulting in double vision in a great majority of cases. (3) The distress from the noise is often unbearable. Our third patient described it as "like a train puffing and roaring all the time" in her head. The distress seems augmented in the stillness of the night, making sleep difficult.

Cures—A cure of the fistulae tends to follow a decrease in the arterial pressure and a slowing of the blood flow within that part of the carotid. It is generally conceded that thrombosis is the cause of the occlusion. This opinion is expressed by many writers, and that cures have resulted from thrombosis of the ophthalmic vein alone supports this theory. Still, in Dorrance's explanation of the results of serial arterial ligation, he says that "cutting down the size of the artery by decreasing the volume of blood it carries should decrease the size of the fistula, with progressive lessening of the columns transported by the proximal artery. Obliteration of its lumen could considerably reduce the size of the fistula sufficiently so as to approximate its edges and permit union."

Spontaneous Cures occur in from 6 to 10 per cent of cases. These may occur soon after the fistula has developed or after many years. The cure results from a thrombus occluding the communicating opening except for the possible occasional occlusion of the opening by scar contracture. Thrombosis is encouraged by slowing of the arterial flow of blood and probably thrombosis occurring from the venous side. A number of recorded cases have resulted in cures following a cellulitis about the affected eye with a thrombophlebitis of the orbital veins. Evidently the thrombosis extended into the cavernous sinus.

Treatment—Treatment has been directed to such procedures as would be expected to promote thrombotic occlusion of the fistula. One of the simpler ones is prolonged compression of the carotid vessels, as well as the venous channels about the eye. Some 16 of 80 cases collected by Keller, deSchweinitz and Sattler were cured by prolonged *compression of the carotids*, and Matas, Locke, and Naffziger have devised mechanical apparatus for prolonged pressure on the carotids. The results from *obstruction of the orbital veins* have not been so favorable. *Subcutaneous injection of gelatin* has resulted in cures in a few cases, but the fear of damage to normal structures has caused it to be used only occasionally.

The *injection of sclerosing drugs* into the ophthalmic veins seems to have been little employed, though, theoretically, this should be expected to be an efficient remedy. The fear of thrombosis extending into the larger venous sinus within the skull has deterred those who have proposed such a remedy. A few injections are reported, but these occurred long ago and were with substances of uncertain sclerosing power. The extensive practice of thrombosing varicose veins at the present time with various drugs with success, probably gives us sufficient experience to use them in this way with success and less danger. The current of blood in the veins is flowing away from the fistula, therefore, the injection is against the current, and the solution will not pass easily along the ophthalmic in the direction of the sinus. We found the attempts at injecting sclerosing solutions anxious procedures, though the outcome was quite satisfactory, and we should not hesitate to inject sodium morrhuate into the ophthalmic vein again if the occasion arose. It should be more effective and a safer procedure than dissection of the veins.

Operative Treatment—The following procedures have been carried out for treatment of pulsating exophthalmos

- (1) Obstruction of the carotids extracranially with ligatures, metal bands, and fascia, partially or completely This may take the form of
 - (a) Ligation of the common carotid alone or preceding ligation of the internal carotid or external carotid on the same side,
 - (b) Primary ligation of the internal carotids,
 - (c) Ligation of both carotids, usually at intervals,
 - (d) Intracranial occlusion of the internal carotid after extracranial ligation
- (2) Plugging the fistula itself with muscle by inserting it in the internal carotid in the neck (Brooks, Homby and Gardner)
- (3) Excision of the ophthalmic veins through the orbit
- (4) Evacuation of orbital contents and attacking the fistula at the apex of the orbit

Beginning with Travers' ligation of the common carotid upon his patient, in 1809, arterial occlusion has been by far the method most often selected for the treatment of this condition Improvement invariably follows one or more of these procedures, but often it is only temporary Cures have resulted in some 60 per cent of cases by carotid ligations in the neck (Locke) Intracranial ligation will increase the number of cures

The *dangers to the brain from the ligation of the larger arteries* are well recognized Weyth, in 1888, reports a mortality of 40 per cent following carotid ligation Matas reports 80 cases of ligation of the common or internal carotids with 11 per cent showing cerebral complications and 75 per cent mortality

Dandy says that "after the age of 35 one should regard total ligation of either common or internal carotid artery as a potential cause of death or cerebral disability, and therefore to be undertaken only after testing the collateral circulation beforehand or otherwise when the occasion leaves no escape After age 60 or even 50, few total ligations are possible without disastrous consequences"

The age of the patient is generally considered an important factor Still, Reid says "We believe that the older patients are, the less likelihood there is of cerebral disturbance following ligation of the carotid artery—certainly our experience has been that it is safer to ligate the carotid vessels in older people than in young people"

These dangers may be lessened by gradual or intermittent occlusion of the vessels over several weeks' time The ligation of the common carotid, followed after a few weeks' interval by ligating the corresponding internal, is less hazardous than primary ligation of the internal Bilateral ligation of both common carotids has been too often fatal to be advised

Intracranial ligations are quite feasible and should not be condemned They have been disappointing, in that cures have not always followed, though

great improvement does result. If one could be sure that the muscle plug inserted in the carotid in the neck would not reach the circle of Willis, it would be a most direct and logical remedy.

CONCLUSIONS

With our present knowledge and experience, we would suggest the following line of treatment for carotid-cavernous fistula.

(1) The common carotid in the neck should be compressed for a period of time. This procedure may cure the spontaneous type or make ligation of the common carotid safer.

(2) The common carotid should next be ligated.

(3) If this is unsuccessful, after waiting a few weeks, the internal carotid should be occluded. At the same time separate branches of the external carotid on the same side should be ligated.

(4) Should symptoms persist, one has the choice of intracranial occlusion of the internal carotid, or

(5) Injection of the ophthalmic veins with sclerosing solutions such as sodium morrhuate. This should be a useful procedure and we would be inclined to give it preference. However, further experience will be necessary before its true value is determined.

(6) Ligation of the opposite external carotid will markedly influence the circulation through the fistula, and since it is without danger, it should be included as a late remedy in reducing the collateral circulation to the ophthalmic artery.

I wish to acknowledge with thanks my indebtedness to my associate, Dr S. R. Snodgrass, for his skillful exposure of the carotid artery within the skull to which the silver clip was applied.

BIBLIOGRAPHY

- ¹ Brooks, Barney. Discussion of Pulsating Exophthalmos, the Result of Injury, by Lloyd Nolan and A. S. Taylor. *South Surg Trans*, 43, 176, 1930.
- ² Dandy, W. E. Carotid-Cavernous Aneurysms. *Zentralbl f Neurochir*, 2, 77, 165, 1937.
- ³ deSchweinitz, G. E., and Holloway, T. B. Pulsating Exophthalmos. W. B. Saunders Co., Philadelphia, 1908.
- ⁴ Dorrance, G. M., and Loudenslager. Physiological Considerations in the Treatment of Pulsating Exophthalmos. *Amer Jour Ophth*, 17, 1099, 1934.
- ⁵ Hamby, W. B., and Gardner, W. J. Treatment of Pulsating Exophthalmos. *Arch Surg*, 27, 676, 1933.
- ⁶ Holman, E. Arteriovenous Fistula. *Arch Surg*, 18, 1672, 1933.
- ⁷ Keller, Emil. Beitrag zur Kasuistik des Exophthalmos, Pulsans. Orell Fussli, Zurich, 1898.
- ⁸ Locke, Chas. E., Jr. Intracranial Arteriovenous Aneurysm or Pulsating Exophthalmos. *ANNALS OF SURGERY*, 80, 1, 1924.
- ⁹ Matas, R., and Allen, C. W. Occlusion of Large Surgical Arteries with Removable Metallic Bands to Test the Efficiency of the Collateral Circulation. *J A M A*, 56, 233, 1911.
- ¹⁰ Matas, R. Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries. *J A M A*, 63, 1441, 1914.

- ¹¹ Matas, R Discussion of Mycotic Aneurysms of the Common Iliac Artery, by Mims Gage *Amer Jour Surg*, **24**, 692, 1934
- ¹² Matas, R Discussion of the Treatment of Carotid Cavernous Arteriovenous Aneurysms, by W E Dandy *Trans Amer Surg Assn*, **53**, 432, 1935
- ¹³ Naffziger, H C Discussion of the Treatment of Carotid Cavernous Arteriovenous Aneurysms, by W E Dandy *Trans Amer Surg Assn*, **53**, 436, 1935
- ¹⁴ Nolan, L, and Taylor, A S Pulsating Exophthalmos, the Result of Injury *South Surg Trans*, **43**, 176, 1930
- ¹⁵ Reid, M R Studies on Abnormal Arteriovenous Communications, Acquired and Congenital *Arch Surg*, **10**, 601, 1925
- ¹⁶ Reid, M R The Treatment of Abnormal Arteriovenous Communications *Arch Surg*, **11**, 237, 1925
- ¹⁷ Reid, M R Discussion of the Treatment of Carotid Cavernous Arteriovenous Aneurysms, by W E Dandy *Trans Amer Surg Assn*, **53**, 437, 1935
- ¹⁸ Sattler, H *Über ein neues Verfahren bei der Behandlung des pulsierenden Exophthalmus* *Klin Monatsbl f Augenheilk*, **43**, 1, 1905
- ¹⁹ Sattler, C H *Pulsating Exophthalmus* *Handbuch der gesamten Augenheilkunde*, Julius Springer, Berlin, 1920

DISCUSSION—DR MONT R REID (Cincinnati, Ohio) As complementary to Doctor Singleton's paper it might be interesting to cite a case which is very similar to the second case he reported. The patient, female, age 11, was first operated upon by Doctor Halsted in 1911. She presented an extensive sinusoid condition about the right ear, mastoid and face, associated with a "noise" in the head and a slight exophthalmos. At this operation, a very large external carotid artery was found. This was ligated and many large veins were excised. Some large arteriovenous fistulae were definitely identified. This operation was followed by a period of marked improvement, but after the lapse of seven years the condition was essentially the same as before this first operation. At the second operation I found the ascending pharyngeal, which was noted to be very small at the first operation, to be as large as a normal external carotid artery. It was ligated and other large veins were excised. For a period of four years, the condition was markedly improved, but after the lapse of eight years, I was informed that the external appearance was essentially the same as before the last operation, although the bruits and thrills were less marked and the patient was not annoyed by noises in the head.

Doctor Singleton's third case illustrates the usual futility of ligating the common carotid artery for a traumatic cavernous sinus-carotid arteriovenous aneurysm. When this is done, there is an immediate reversal of blood flow in the external carotid artery, and a large amount of blood flows backward to the bifurcation and thence upward through the internal carotid artery to keep the fistula alive and active. To avoid this, I have for many years advocated ligating the external carotid artery and occluding the common carotid with an aluminum band. This gives the maximum reduction of blood flow through the fistula and also the precaution of being able to remove easily the aluminum band and restore circulation should cerebral symptoms develop. His fourth case illustrates beautifully the additional advantage of ligating and sclerosing the supra-orbital veins in addition to the work upon the arteries of the neck.

In support of this argument, I am permitted by Dr Frank Mayfield, of Cincinnati, to refer to one of his cases. It was a typical instance of traumatic pulsating exophthalmos. A ligation of the common carotid artery was followed by a very transitory improvement and then a rapid return of all symp-

toms and signs. A subsequent ligation of the external carotid artery was followed by so much improvement that the patient was not conscious of any bruit, although it could be heard through the stethoscope. Later, a division and thrombosis of the supra-orbital vein was followed by a complete cure. All of these operations could have been performed at one time although, as done in stages, the risk of central disturbances may have been lessened. However, when the maximum reduction of blood flow through such a fistula is sudden, the incidence of cures is certain to be higher.

I am glad that Doctor Singleton has called attention to the fact that spontaneous cures of traumatic pulsating exophthalmos do occur. He estimates the incidence from 6 to 10 per cent. Could not this incidence be increased by putting our patients to bed in the Fowler's position and instituting other measures to reduce the amount of blood flow through the fistula?

Doctor Singleton's report of a case in which he ligated the opposite external carotid artery after doing all he could on the side of the fistula is most interesting. This opens up another therapeutic procedure which may, if necessary, be brought into action in the treatment of this difficult problem of intra- and extracranial cirroid aneurysms. In the first case I cited, it seems obvious that this procedure should have been done, inasmuch as four years after the last operation temporary occlusion of the left common carotid artery affected the bruit as much as did occlusion of the right vessel.

DR GILBERT HORRAX (Boston). My experience has been almost entirely with the cirroid type of lesion in the brain. In two or three instances we have turned down a bone flap and exposed such a cirroid aneurysm. These lesions, of course, extend below the surface, and spread out over the cortex throughout a wide area.

The patients upon whom we have performed this operation have suffered from epilepsy of one type or another, or possibly from other intracranial symptoms, and what we have done at the time of operation is to seal off by electrocoagulation a large number of the great venous trunks. They will shivel up with the coagulating current very well, and you can effect a very extensive coagulation in that way. Whether or not that is going to prove efficacious in stopping the spread or the increase in size of these blood vessels, I am not sure, but so far the attacks have been diminished.

DR GEORGE J HEUER (New York, N. Y.). In the hope of provoking further discussion of the treatment of the intracranial cirroid aneurysms involving the cerebral cortex, I should like briefly to refer to six cases of this condition seen during the past few years. The patients presented themselves because of headaches, convulsions, transient hemiparesis or noises in the head. Two were young children, two young people of 14 and 20, two adults of 40 and 43. In none was there a history of injury to account for the condition. All, on auscultation, presented loud bruits either over one side or over the entire head. Ventriculograms in five of the six cases showed slight displacement or distortion of the ventricle on the side of the lesion, but of course failed to give any information regarding the extent of the lesion. An attempt to delineate the extent of the lesion by the use of thorotrast was made in three cases. In one, it was successful, and no harm followed its employment.

Our treatment of these patients as yet may be spoken of as tentative or palliative and it is for this reason we should be grateful for suggestions. In two of the cases, we have performed ligation either of the right or left external and common carotid arteries. The result in one has been steady improvement, in the other, slight if any improvement. In two cases, a cranial exploration and decompression was combined with the administration of from 3,600

R units to 9,600 R units of roentgenotherapy. In one case, the headaches have improved and the frequent convulsive seizures reduced to one during the past three years, in the other cases, there has not been any improvement. In one case, a cranial exploration and decompression was followed by ligation of the right external and common carotid arteries and the administration of 13,000 R units of roentgenotherapy. The result has been a diminution in the number of convulsive seizures. One case thus far has refused treatment. These cases will be reported in more detail at a later date.

DR WILLIAM JASON MIXTER (Boston) It seems to me that Doctor Singleton has given us a very concise account of the handling of two quite distinct groups of cases, because the arteriovenous aneurysms of the cavernous sinus must be considered quite separately from the cirroid aneurysms of the cranium or the brain.

I should think that his plan of action in regard to the cavernous aneurysms was excellent. I do not know whether I would agree with him absolutely in his choice of the last two methods, because I am rather afraid of sclerosing solutions in a place like the ophthalmic veins, nevertheless, his result in this case has been so good that I think he has the right to prefer it.

As regards the other group of cases which he mentioned, the two cirroid aneurysms, there we are dealing with a different problem, and we have to evaluate each particular case very much on its own merits according to the structures involved.

In one of his cases, the first, there was evidently considerable involvement of the cerebrum, and I wonder whether the boy's paralysis was due entirely to the ligation of the carotid or whether it was simply from progress of the lesion in the cerebrum.

These cases require a tremendous amount of care in recognizing the vessels involved, and I think the only thing that I would suggest would be the use of thiocontrast, which in such cases as this is of great value in demonstrating where the larger trunks lie.

DR FRANCIS GRANT (Philadelphia) With regard to Doctor Singleton's problem of exophthalmos on the side of the aneurysm, we have recently had a case in which the boy had been relieved by external ligation of various carotid vessels, and consequent upon that the exophthalmos had continued with the venous engorgement. We explored that case for the possibility of either clipping the carotid intracranially or getting rid of the vein, and we took off the roof of the orbit. I have had occasion to do that once or twice for orbital tumors. It is a very simple thing to do. In this particular case the vein was engorged in the orbit and it was a relatively simple matter to ligate them in that area. Furthermore, I think with the removal of the roof of the orbit the exophthalmos tends to decrease because you obtain decompression upward into the cranium. The exposure that you employ would be precisely that for ligation of the carotid intracranially, and, as I say, the removal of the orbital roof is not particularly difficult. So if you happen to be faced with one of these problems of enlarged veins, that would seem to be a possibility for its control.

DR ALBERT O SINGLETON (closing) I am very glad to have these able discussions recorded with this paper.

The real object of treatment is to occlude the sinus. In the carotid-cavernous cases, which are the ones that have created so much interest, it is a thrombosis that stops the fistula. If one can slow the blood stream enough to allow clotting to occur, there is a cure. This usually is attempted by an

attack upon the arteries, but, as Doctor Reid pointed out, a complete stopping of the circulation through the carotid, that portion where the fistula is located, is apt to result in cerebral symptoms of a severe nature

The observations are that many of these patients have been cured by thrombosis of the ophthalmic vein, as in cellulitis, or thrombophlebitis, and apparently the thrombosis does not extend back farther than the cavernous sinus, or far enough into the venous sinuses to be of great danger to the venous circulation in the brain

So I am strongly of the opinion that the injection of sclerosing solutions into the ophthalmic veins will prove to be a very useful remedy in the treatment of this condition. The current of blood is running away from the brain and will not carry the solution into the cavernous sinus. If thrombosis can be started in the ophthalmic veins, it may, as in this case, extend back to the sinus and occlude the fistula without endangering the circulation

MYASTHENIA GRAVIS AND TUMORS OF THE THYMIC REGION*

REPORT OF A CASE IN WHICH THE TUMOR WAS REMOVED

ALFRED BLALOCK, M D , M F MASON, PH D , HUGH J MORGAN, M D ,
AND S S RIVEN, M D

NASHVILLE, TENN

FROM THE DEPARTMENTS OF SURGERY, MEDICINE AND BIOCHEMISTRY VANDERBILT UNIVERSITY SCHOOL OF MEDICINE,
NASHVILLE, TENN

THIS PAPER deals in the main with myasthenia gravis and certain abnormalities of the thymus, and the possible relationships of these conditions to each other. It is recognized that any consideration of these subjects must be limited in scope because of the incompleteness of our knowledge. With regard to tumors of the thymus Ewing¹ states "No group of tumors has more successfully resisted attempts at interpretation and classification than those of the thymus. The problems involved include those which have complicated the embryologic and histologic study of the gland, while added difficulties arise from the comparative rarity and considerable diversity of the tumors, and from the somewhat imperfect knowledge of the general pathology of the thymus." Thus, we wish to emphasize, at the beginning, that knowledge concerning myasthenia gravis and thymic tumors, and the relationship of these to each other, is relatively meager.

Myasthenia Gravis—Myasthenia gravis is a disease characterized by abnormal fatigability of muscles, usually, but not always, attended by characteristic lymphocytic infiltration of these and other organs,² and frequently by abnormalities of the thymus, such as failure of involution and neoplasms^{3, 4}. There are no characteristic or constant lesions of the central nervous system. The occurrence of spontaneous remissions indicates that whatever the underlying disorder may be, the changes it produces are not irreversible in nature.

Norris⁵ recently stated "Historically, myasthenia gravis has been regarded from widely differing points of view. At first it was believed to be a disease of the central nervous system, then regarded as an entity whose picture was produced by metastases from a malignant thymus, and then as a primary disease of the striated musculature of the body. Our point of view then seemed to be changing toward classifying it among the diseases of general metabolism, and finally the malady seems to be best regarded as a disturbance of the neuromuscular mechanism, possibly upon an endocrine basis." The prevailing theory at the present time is that there is in myasthenia gravis some interference with the transmission of impulses across the myoneural junction. However this may be, the precise etiology of the disease is unknown. The mechanism underlying its most outspoken manifestations, weakness and abnormally rapid fatigability of muscles, is poorly

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

understood. Yet, in spite of this lack of knowledge, certain drugs have been employed in its treatment with a moderate degree of success. Among these are ephedrine, glycine, prostigmin and guanidine.⁶ The response to prostigmin, in terms of temporarily improved muscle strength and endurance, has been found to be so constant that a therapeutic test with this drug is considered the best diagnostic sign of myasthenia gravis.⁷

Tumors of the Thymus—An excellent description of the variations in structure which may be encountered in thymic tumors is given by Ewing.¹ He stated "A full survey of the structural variations reveals, at one extreme, a mixed process involving lymphocytes and reticulum cells, with giant, plasma, and eosinophile cells, producing a structure nearly identical with Hodgkin's granuloma. At the other extreme, are nearly pure tumors of rounded or polyhedral reticulum cells, i.e., lymphosarcoma and carcinoma."

Hence the conclusion is reached that the great majority of the thymus tumors, and especially the mixed growths, represent infectious granulomata, or particular forms of cell overgrowth arising on the basis of an infectious granuloma." Since tumors of the thymic region are relatively uncommon, and as one observer usually has the opportunity to study only a few lesions and because there is this difficulty in interpretation of the structure, it is not surprising that various points of view concerning the nature of the tumors have been expressed. Regarding nomenclature, Decker⁸ stated "Thus by thymoma, Brown means carcinoma, Ciotti all tumors, Bell nonmalignant tumors, Margolis all tumors of parenchymal origin." It is generally agreed that benign tumors of the thymus are encountered less frequently than malignant ones. Crosby⁹ published, in 1932, a review of all malignant tumors of the thymus reported up until that time. The total number was 166, 122 of which he classified as sarcomata and 44 as carcinomata. The review of malignant tumors of the thymus was brought up to date by Decker,⁸ in 1935, at which time the total number was 208. Several have been recorded since that time. Reports of benign tumors of the thymus are few in number and in most instances they have occurred in patients with myasthenia gravis.

Abnormalities of the Thymus and Myasthenia Gravis—That there may be more than a casual relationship between myasthenia gravis and abnormalities of the thymus is suggested by their frequent association. The first description of a thymic tumor in association with myasthenia gravis was reported by Weigert,³ in 1901. Bell⁴ collected, from the literature of 1901-1917, 56 cases of myasthenia gravis in which autopsies or operations had been performed. Twenty-seven of these exhibited abnormalities of the thymus. A diagnosis of thymoma was made in ten and the remainder were recorded as having either a persistent or an enlarged thymus. The tabulation was continued by Norris⁵ and brought up to 1936. Among a total of 80 necropsy reports on patients with myasthenia gravis, including those of Bell, 35 record lesions of the thymus. He stated "I am of the opinion that pathologic changes may be found in the thymus in cases of myasthenia gravis in direct ratio to the care with which they are sought." A careful search

TABLE I
 LESIONS OF THE THYMUS IN MYASTHENIA GRAVIS
 (Collected by Bell⁴ and Norris⁵)

Case No	Year	Author	Patient		Thymus	
			Age	Sex	Enlarged or Persistent	Tumor
1	1901	Laquer and Weigert	30	M		5x5x3 cm
2	1901	Weigert	—	—		A tumor
3	1901	Burr and MacCarthy	21	F	Enlarged	
4	1902	Hödlmoser	18	F	Enlarged	
5	1902	Link	43	M	3 cm long	
6	1904	Hun, Blumer and Streeter	32	M		5x5x5 cm
7	1905	Burr	30	M	22 Gm	
8	1905	Buzzard	40	M	9.5 Gm	
9	1905	Buzzard	40	M	59.4 Gm	
10	1905	Buzzard	28	F	41 Gm	
11	1905	Dupré and Pagniez	32	F	8 Gm, persistent	
12	1907	Steinert	Elderly	F	Persistent	
13	1908	Meyer	47	M	Enlarged	
14	1908	Booth	11	M	11x5.5x1 cm	
15	1908	Marinesco	31	F	Persistent	
16	1908	Mandlebaum and Celler	52	M		5x3.5x2 cm, 20 Gm
17	1908	Wiener	67	F		A tumor
18	1908	Meggendorfer	47	M		A tumor
19	1909	Boudon	17	F	36 Gm	
20	1911	Moorhead	25	F	Persistent	
21	1911	Symes	21	F	11.4 x 7.6 cm	
22	1911	Oppenheim	40	F		A tumor
23	1912	Klose	23	M		A tumor
24	1913	Schumacher and Roth	19	F	49 Gm	
25	1914	Claude, Géry and Porak	51	M		A tumor
26	1915	Hart	—	—		5x4x4 cm
27	1915	Hart	30	F	Persistent	
28	1917	Bell	58	M		6x3.6x3.5 cm, 60 Gm
29	1921	Bouttiet and Bertrand	Mid age	F	Persistent	
30	1923	Mella	48	M		7.5x5.5x2.5 cm
31	1929	Alter and Osnato	31	F		9x7x6 cm
32	1934	Brem and Wechsler	27	F		4x2.5 cm
33	1934	Brem and Wechsler	54	M		9x3 cm

TUMORS OF THYMUS

TABLE I (Continued)

Case No	Year	Author	Patient		Thymus	
			Age	Sex	Enlarged or Persistent	Tumor
34	1936	Norris	37	F		10x4x4 cm , 57 Gm
35	1936	Norris	33	M		5 8x4 8x1 2 cm , 16 6 Gm
(Collected by Authors)						
36	1918	Froboese-Thiele and Lesch- ziner	27	F	Persistent 15 Gm	
37	1919	Pulay	17	F	Enlarged	
38	1923	Mott and Barrada	—	M	70 Gm Thick fibrous cap- sule	
39	1930	Auerbach	53	F		Pigeon-egg in size
40	1931	Halpern and Popper	43	F		9x5x5 Encapsu- lated
41	1932	Lowenthal	63	F	Enlarged 26 Gm 8x4 5x 1 5 cm.	
42	1932	Symmers (Case 14)	52	M		12 5x7 5x2 5 cm Smooth
43	1933	Zajewloschin	30	F		5x4x1 4 cm
44	1935	Gold	31	F		4 cm in diameter. Round tumor
45	1936	Butt	—	—		Tumor
46	1936	Butt	—	—		Tumor
47	1936	Alajouanine, Hornet, Thurel and Andre	40	M.		Large Tumor
48	1937	Alajouanine, Hornet and Morax	48	M		Ovoid tumor Size small hen's egg
49	1937	Norris	52	M		63 Gm 9x6x3 5 cm Numerous cysts
50	1937	Adler	40	F		Size of child's head Opera- tion Death
51	1937	Obiditsch	50	M		7x4x3 cm.
52	1937	Obiditsch	47	M		Size of man's fist Operation Death
53	1938	Peer and Farniacci	20	M.		136 Gm 12x6 5x 3 5 cm
54	1939	Authors' case	24	F		Cystic tumor, 6x5x3 cm

of the literature has resulted in the collection of 18 additional cases¹⁰ to 26 of myasthenia gravis with abnormalities of the thymus, determined by autopsy or operation. Most of these have been reported since 1935. Thus, there have been reported 53 instances of abnormalities of the thymus in approximately 110 autopsies or operations upon patients with myasthenia gravis. Thirty-one of these are classified as tumors and 22 are recorded as exhibiting enlargement or persistence of the thymus (Table I). It is doubtful if the incidence of the association of myasthenia and abnormalities of the thymus is as high as these figures indicate, since the autopsy findings in patients with myasthenia are more apt to be reported if there is present some abnormality such as a tumor of the thymic region. On the other hand, it is possible that small tumors may be overlooked at necropsy unless a careful search is made.

In addition to the reports which are listed in Table I, and which are described in the literature in moderate detail, there are a number of casual references to the association of myasthenia gravis and thymic abnormalities. Gordon Holmes²⁶ states that there were either tumors or enlargements of the thymus in six of the eight cases of myasthenia gravis which he had examined at autopsy. Greenfield²⁶ stated that the thymus was persistent in three subjects he examined postmortem. In addition, there are a number of reports on roentgenologic evidence of anterior mediastinal tumors in patients with myasthenia gravis.

The collected series of Norris⁵ (1936) and Lievre²⁷ (1936) do not agree in all respects. Lievre assembled observations on 67 patients with myasthenia in whom complete autopsies were performed. A tumor in the thymic region was found in 24 of these and persistence or hypertrophy of the thymus in 32. No anomaly was noted in the remaining 11 patients. The mean weight of the tumors was 60 Gm and the mean diameter was 5 cm. Their usual location was in the anterior mediastinum, immediately behind the sternum and in contact with the superior part of the pericardium. Lievre, as well as others, has observed that most of the thymic tumors reported in individuals without myasthenia were malignant, whereas a large percentage of the benign ones occurred in myasthenics. One of the exceptions is an "essentially non-malignant" tumor of the thymus weighing 2,235 Gm, reported recently by Andrus and Foot²⁸. A diagnosis of myasthenia was not made in this patient, a boy, age 13, although abnormal fatigability was a prominent symptom.

Bell⁴ stated that the thymic tumors occurring in myasthenia gravis form a distinct group. "They are all comparatively small, benign growth, composed of young thymic tissue. Many are hemorrhagic." Norris⁵,²² is of the opinion that the pathologic findings which are present in the thymus in myasthenia gravis are best interpreted as conditions of greater or lesser degrees of epithelial hyperplasia. "When the hyperplasia is extreme, a localized, and at times encapsulated, tumor-like mass is formed. In these instances of more extreme hyperplasia the usual lobular structure of the thymus may be completely obliterated and only very few lymphocytes and

almost no Hassall's corpuscles may be found in the epithelial mass. On the other hand, when the hyperplasia is considerable but less extreme, the lobulation of the thymus may persist and the corpuscles of Hassall and lymphocytes may be relatively more numerous." Lievie²⁷ states that thymomata contain lymphoid and epithelial elements and rarely Hassall's corpuscles. Biern and Wechsler²⁹ found lymphocytes, plasma cells, large polyhedral cells and occasionally giant cells and Hassall's corpuscles. Obiditsch²⁴ states that there is a preponderance of small round cells in benign tumors of the thymus associated with myasthenia gravis, whereas they are almost entirely epithelial in type in the thymic tumors not associated with myasthenia.

In spite of difficulties in interpreting the classification of thymic tumors, it is our impression that there has been recorded only one case in which myasthenia was associated with a malignant thymic growth. This is the case reported by Meggendorfer,³⁰ in 1908. However, Bell⁴ expresses some doubt concerning the correctness of the classification of this tumor. In any event, it would seem highly probable that hyperplasia or benign tumors of the thymus and myasthenia gravis accompany each other in a large percentage of cases, whereas malignant tumors of the thymus and myasthenia are rarely associated.

Operations upon the Thymus in Patients with Myasthenia Gravis—The literature contains the records of only four attempts to influence the course of myasthenia gravis by surgical intervention. The first of these was reported by Schumacher and Roth,³¹ in 1913. The patient, a female, age 21, had definite and severe hyperthyroidism and myasthenia gravis. There was a symmetrical increase in the size of the thyroid gland with a marked increase in its vascularity. Roentgenologic examination revealed a mass in the anterior mediastinum which was thought to be an enlarged thymus. The first operation consisted of ligation of the right superior thyroid artery and vein. Little if any improvement resulted. The second operation (Sauerbruch) consisted in the removal of an enlarged thymus which weighed 49 Gm. Examination of this gland showed hypertrophy without tumors. The picture was that of a fetal thymus. Hassall's corpuscles were numerous. A diminution in the signs and symptoms of myasthenia followed this operation. A subtotal thyroidectomy was performed 18 months subsequently, following a severe thyroid crisis. The patient improved but was not cured of myasthenia at the time of the report. The second case of myasthenia in which an operation upon the thymus was performed is mentioned very briefly by Haberer³² in a report of operations upon the thymus for other conditions. The patient was a man, age 27. There was no evidence of enlargement of the thymus gland. A partial thymectomy was performed and the thymus was described as being in a state of involution. When examined three years subsequently, the patient appeared to be improved. The third case is reported by Adler.²³ In this instance, a benign thymic tumor the size of a child's head was removed by Sauerbruch. The patient died eight days subsequently of mediastinitis. The fourth case is that reported by Obiditsch,²⁴ in which the

tumor was the size of a man's fist. It was removed by Sauerbruch and the patient died five days later as a result of a Streptococci infection. Lievre,²⁷ in 1936, stated that there existed no published report of the successful removal of a thymoma. Andrus and Foot,²⁸ (1937) in reporting the removal of an "essentially nonmalignant" tumor of the thymus in a boy without myasthenia gravis, states "No case that we can find has survived operative removal of a thymoma more than a few days, which makes our case unique."

Case Report—The complete record of this patient including her preoperative course has been reported in detail by two of us (Riven and Mason³³). Only the salient features will be recounted here.

J. H., white, female, age 19, was referred, in 1934, by Dr. Walter Dandy of Baltimore and Dr. C. D. Walton of Mount Pleasant, Tenn., with a diagnosis of myasthenia gravis. Typical symptoms of this disease appeared at age 16 in February, 1932, and persisted for approximately three months. The muscles of the face, jaws and eyes were involved. The next exacerbation occurred in February, 1933, and persisted for five months. There was difficulty in talking and in using the legs and arms as well as the muscles involved in the first attack. The next recurrence, in February, 1934, was even more severe and symptoms persisted for seven months. She fell a number of times when attempting to walk. She was first seen in the Vanderbilt Hospital in September, 1934, in a partial remission, and the positive findings were limited to the presence of dysfunction of the muscles of expression and some weakness of the muscles of the neck, abdomen and extremities. The basal metabolic rate was normal. Roentgenologic examination of the chest (Dr. C. C. McClure) revealed a sharply circumscribed, dense shadow just anterior to the left auricle, extending somewhat to the left and not seen to the right of the midline. Roentgenotherapy was instituted and the shadow of the mass in the anterior mediastinum decreased in size. Therapy otherwise consisted of ephedrine and glycine. Roentgenotherapy was again administered in January, 1935.

The next severe relapse occurred in December, 1935. She complained of progressive weakness, ptosis of the eyelids, diplopia, indistinct vision and difficulty in talking, chewing and swallowing. The return of these symptoms had been gradual. The facial expression was languid and the speech was slow and slurred. There was partial ptosis of the eyelids. The mouth was drawn to the right and the left side of the face was smoother than the right. The masseter muscles were weak. The grip in the right hand was weaker than that in the left and both hands tired very quickly. The muscles of the trunk and lower extremities became fatigued quite readily. Roentgenologic examinations showed that the mass in the mediastinum had returned to a slightly larger size than that observed prior to the roentgenotherapy.

On December 28, 1935, treatment with drugs was suspended for the purpose of completing certain metabolic studies. Several days later, the condition of the patient became suddenly worse. Prostigmin was administered and dramatic improvement of approximately three hours' duration was obtained. In addition, therapy with glycine and ephedrine was instituted. Increasing amounts of prostigmin became necessary and during the latter part of January, the patient received as much as 9 cc. in 24 hours. On the morning of January 31, 1936, the patient asked that the 5 A.M. dose of prostigmin be omitted. This was done. She was not observed again until 7:15 A.M., at which time she was extremely cyanotic. Respiratory movements were barely perceptible. Vomiting had occurred and she was incontinent of urine and feces. Artificial respiration and prostigmin therapy were instituted and normal breathing was resumed in approximately ten minutes.

During February, the patient received a course of four roentgen ray treatments over the region of the thymus but this did not cause any decrease in the size of the mediastinal shadow or any immediate improvement early in March. Less prostigmin was required and the dose was reduced gradually. During April, the patient was able to be out of

TUMORS OF THYMUS

bed most of each day. She gained in weight and strength. By May, she was considered to have attained a good remission.

Dr. Barney Brooks and Dr. Edward Churchill were consulted, and it was agreed that the tumor mass in the anterior mediastinum should be removed. Because of the marked incapacity the patient had experienced, because it seemed possible that removal of the tumor might result in improvement, and because the risk inherent in the operative procedure was judged to be not great, this course was decided upon.

Operation—May 26, 1936 (Doctor Blalock). An intratracheal tube was introduced and the anesthesia consisted of nitrous oxide and oxygen and a small amount of ether. An incision was made beginning in the suprasternal notch, extending down the midline of the sternum and curving slightly to the right at the third interspace. By the use of sharp and blunt dissection, an index finger was introduced through the suprasternal notch beneath the sternum into the anterior mediastinum. By a similar procedure, an index finger was introduced beneath the sternum through the third right interspace. After pushing the pleura and other structures laterally, the sternum was split in the midline with shears. It was cut across in a transverse direction at the level of the third interspace.



FIG. 1.—Photograph of tumor, measuring approximately 6.5 x 3 cm, removed from thymic region.

A self-retaining retractor was inserted and a good exposure of the anterior mediastinum was obtained. A reddish-purple tumor was visible in the thymic region. It was densely adherent to the neighboring structures. By sharp and blunt dissection it was freed from the surrounding structures and the vessels at its base were ligated with silk. The tumor was regular in outline and was soft. No other abnormalities were visualized. Some of the tissues surrounding the tumor had the appearance of fat. No tissue was definitely identified as being thymus. The space left by the removal of the tumor was obliterated in part by suturing the neighboring structures together. Several holes were made in the sternum by the use of a drill and the opposite sides were approximated with catgut sutures. The third and fourth costal cartilages were approximated by an encircling suture of catgut. The anterior periosteum of the sternum was closed with interrupted silk sutures. Similar sutures were used in closing the subcutaneous tissues and skin. One cubic centimeter of prostigmin was administered before the operation was begun and a second dose was given during the course of the operation. There were no untoward incidents during the operative procedure and the patient was returned to the ward in good condition.

Pathologic Examination—Gross. The cystic tumor was quite evidently benign. It was smooth, well encapsulated and measured approximately 6.5 x 3 cm (Fig. 1). Its wall varied from 4 to 8 mm in thickness. It contained thin, brown fluid and shreds of brown, seminecrotic material.

Sections of the tumor were studied by Dr E W Goodpasture and the following is from his report

Microscopically, "the sections show a fibrous wall lining a somewhat spherical mass, the interior of which, so far as can be judged from the small portions attached to the fibrous wall, is composed of fibrin, red cells and precipitated protein. There is no evidence in these sections that there are remnants of a previously organized tissue which has undergone necrosis. The fibrous wall consists of essentially three layers. An outer thin adventitial layer in which there are fairly large blood vessels, both arteries and veins. Here and there are extravasations of red blood cells and about some of the smaller vessels there is an accumulation of lymphocytes and plasma cells. Underlying this coat there is a dense hyaline collagenous membrane arranged more or less in laminations measuring about one millimeter in thickness through which traverse a few blood vessels. Some of the arteries in this layer show an endarteritis with thickening of the intima which encroaches upon the lumen. Beneath this second coat of hyalinized fibrous tissue, there is a layer of granulation tissue of varying thickness and degrees of degeneration. In some areas of the granulating layer there are foci of degeneration in which clefts formed by cholesterol crystals remain. Some of these spaces have no reaction about them, others are lined by mononuclear phagocytes or foreign body giant cells. Frequently about such areas the granulation tissue is filled with "foam cells" representing phagocytes previously filled with lipid materials. In still other areas there is a considerable amount of orange amorphous pigment representing hemosiderin. Occasionally, small deposits of calcium are also noted. There is very little cellular exudate within the granular layer although there are numerous focal accumulations, usually perivascular, of plasma cells intermixed with lymphocytes. Blood vessels and capillaries are numerous and they extend inwardly into the fibrinous material which is being organized thereby (Figs 2, 3 and 4).

"In no section which I have examined is there microscopic evidence of thymic tissue of any sort nor of any other previously organized tissue.

"It would appear that the encapsulated mass had been distended by extravasated blood, consisting of red blood cells, fibrin and serum, which is gradually becoming organized by granulation tissue.

"Aside from the history and location of the mass the only diagnosis that I can make from the examination of the microscopic section is. An encapsulated fibrino-serosanguineous exudate, degenerative changes in the capsule indicated by hyalinization, necrosis, cholesterol crystal deposits, foreign body reaction, hemosiderin pigmentation, slight calcification, hyalinization of connective tissue, and endarteritis at times obliterating. The etiology is not evident.

"In attempting to interpret the pathologic picture present, it seems quite likely from the position of the mass and from clinical relationships that it represents the remains of a necrotic thymic tumor. The necrosis and fibrosis might reasonably be explained on the basis of roentgen ray irradiation."

The patient had a very smooth postoperative course. Prostigmin was administered in small amounts for the first eight days following the operation and it was then discontinued. She was transferred to the medical service 12 days following operation and she was discharged from the hospital on the twenty-first day.

Subsequent Course—A part of the first winter following the operation was spent in Florida where she remained for four and one-half months. Her tolerance to exercise was rather poor when she arrived there but this improved rapidly and very shortly she was able to swim and dance. She would often walk as much as ten miles a day. She would occasionally, once every month or two, take a little prostigmin by mouth. This was usually on occasions when she had exercised a great deal during the day and was going to a dance at night. She returned to Nashville, March 30, 1937. The striking difference noted at that time was that her smile appeared essentially normal. There was perhaps a slightly drawn expression around the nose which had persisted.

She contracted a severe respiratory infection shortly following her return from Florida and she noted some difficulty in masticating her food and there was a less notice-

TUMORS OF THYMUS

Fig 2—Photomicrograph showing wall of cystic cavity. From above downward: dense hyaline collagenous layer of granulation tissue, fibrin and eosin (Hematoxylin and eosin) (X35)

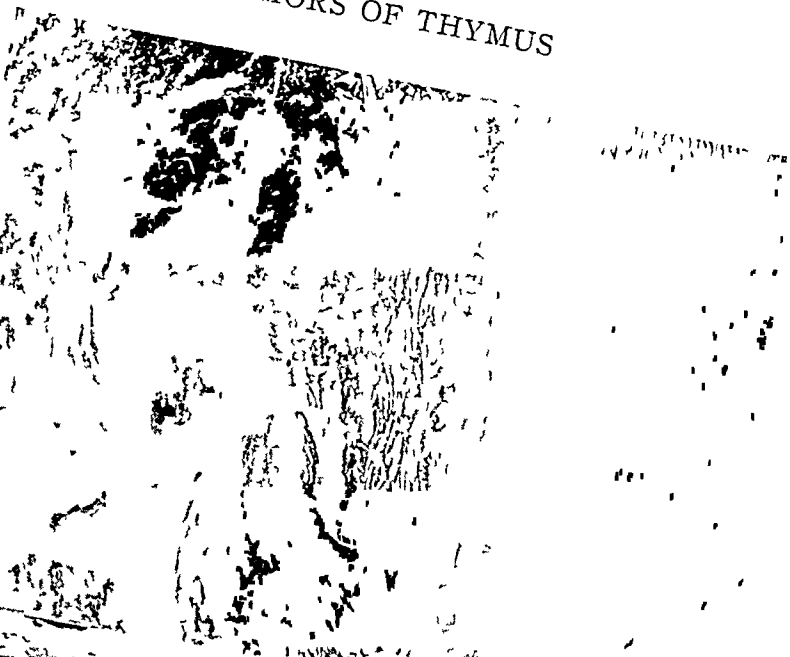


Fig 3—Photomicrograph showing cholesterol deposits (foam cells and endarteritis) (left lower part of field) (Hematoxylin and eosin) (X44)



Fig 4—Photomicrograph showing, from above downward, lymphocytes and plasma cells (some rounded by foreign body vessels, cholesterol clefts) surrounded by granulation tissue (Hematoxylin and eosin) (X120)

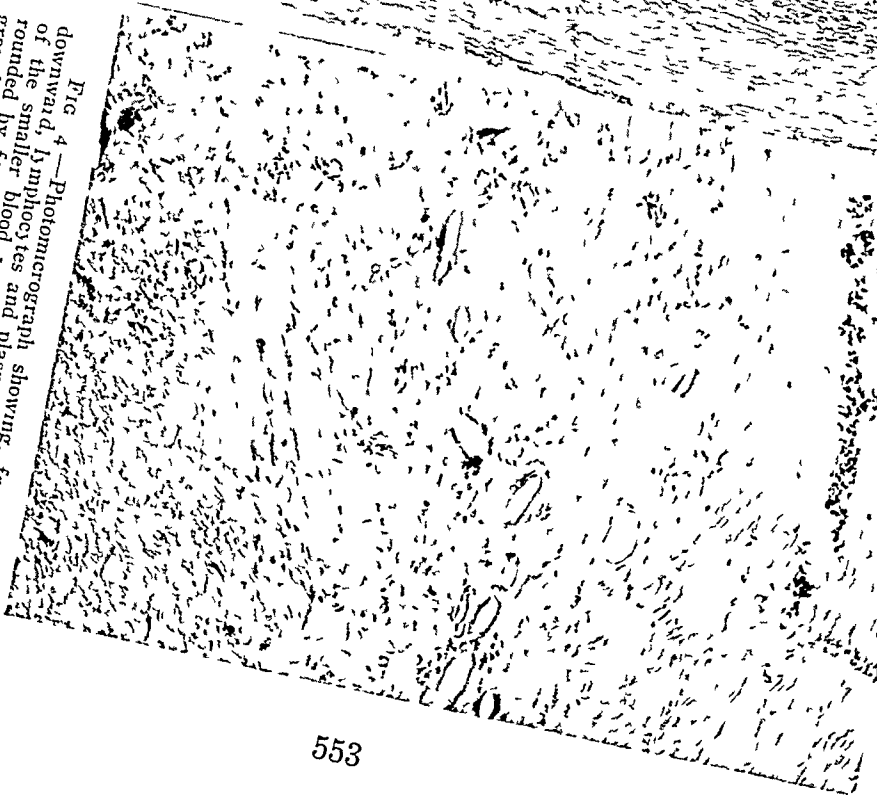




FIG 5—Preoperative, lateral roentgenogram of chest showing tumor in anterior mediastinum



FIG 6—Lateral roentgenogram taken one year following the removal of the tumor



FIG 7—Photograph of patient taken two weeks following the operation



FIG 8—Photograph of patient taken one year following the operation

able return of some of her other symptoms. She returned to the hospital for a stay of two days. The symptoms cleared up in a short while.

For the past two years, there has been no recurrence of symptoms. She has not gone to a warmer climate during the winter, spending one winter in Washington, D. C., and one in Virginia without a return of symptoms of myasthenia. On a few occasions she took a small quantity of prostigmin by mouth before undertaking severe exercise such as a game of tennis. During recent months she has not taken prostigmin on any occasions.

Roentgenograms of the chest before and after operation are shown in Figures 5 and 6. Unfortunately, a preoperative photograph of the patient cannot be located. A photograph taken two weeks following the operation and another taken a year subsequently are shown in Figures 7 and 8.

In summary, during the three years following the removal of a tumor of the thymus region, a patient who had been incapacitated for months every year for four years has had only one mild recurrence which lasted only a few days. This was associated with a severe respiratory infection.

Discussion—It is generally agreed that the thymus, at least in the adult, is a nonessential organ. For this reason, we felt that the chief question to be decided in considering operation in our case was whether or not the possible gain was sufficient to justify the risk associated with the major operative procedure. Although there is no unanimity of opinion concerning the physiologic functions of the thymus, some of the views on this subject will be discussed.

Five general methods of study of thymic function have been employed, in which the effects of the following procedures upon various experimental subjects have been observed: (1) Removal or destruction of part or all of the gland at various ages, (2) excessive feeding of thymic tissue or extracts, (3) multiple injections of extracts of the organ, (4) implantation of additional thymic tissue, and (5) combinations of these methods. In addition, the effects on the thymus of induced alterations in the other ductless glands have been noted. Present knowledge with respect to the first four categories may be summarized as follows:

(1) *Effects of Removal or Destruction of the Thymus*—An extensive literature upon this subject has developed since the original experiments of Restell,³⁴ in 1845, from which only one conclusion may be drawn with certainty, *i e.*, the thymus is not essential to life. The findings of Basch,³⁵ Klose and Vogt,³⁶ and Matti³⁷ that thymectomy led to abnormalities in calcium metabolism were shown in the excellent study and review of Park and McClure³⁸ to be the result of the diet and confinement in a cage rather than the direct consequences of thymic extirpation. The numerous claims that the gonads were affected by thymectomy have been dealt with in a critical review by Anderson.³⁹ From a careful study of the literature, and from extensive experimental data of her own, she felt able to state: "We may conclude that thymectomy does not prevent, hasten, or delay the arrival of sexual maturity, and it does not prevent the occurrence of normal litters. In other words, aside from the immediate effects of the operative injury, it has not been shown that deprivation of the thymus, even in early life, has any effect upon the development and function of the sexual apparatus." In

her own experiments with rats one series was thymectomized at the age of one day

Andersen's point of view may need modification in the light of some of the more recent evidence. Thus Shay *et al*^{40 54 55} have destroyed the thymus of young rats by ionizing rays and find that there is an arrest in the development of the spermatogenic portion of the testes, leading to physiologic castration, with castrate changes in the pituitary. The changes progress until about the one hundredth day of life during which time the males are sterile. After this period, reparative processes occur, fertility returns, and the testes and pituitary are normal again at 150 days. The reparative processes set in about the time the thymus passes the peak of its development and commences involution. Females were not affected.

Einhorn and Rowntree^{41, 42} studied the effects of thymectomy upon successive generations of rats and obtained retardation of growth, and to a lesser extent, somatic development, commencing in the second (F_1) generation, and becoming more pronounced thereafter. Only a limited period of growth is affected (ten to 50 days), the rats operated upon eventually attaining the same size as controls. All thymectomies were performed at from 17 to 24 days of age and the glands of both parents had to be ablated in order to secure the observed effects.⁴² In any given generation, the growth curves of thymectomized and nonthymectomized litter mates are the same. No definite interpretation has been advanced for this curious cumulative effect which is the reverse of that resulting from injection of thymus extract (*vide infra*).

(2) *Excessive Feeding of Thymic Tissue or Extracts*—The literature on this phase of thymus physiology is summarized by Gudeimatsch,⁴³ who made the first observations on the effect of feeding thymic tissue and obtained improved growth and retarded metamorphosis in tadpoles. In the case of rats, improved growth but no retardation of differentiation was observed. Similar results were obtained by Ratti.⁴⁴ The objection that these results are simply due to improved nutrition is rendered unlikely by the fact that injected purified extracts of thymus increase growth (*vide infra*).

(3) *Effects of Multiple Injections of Thymic Extracts*—The first experiments in this category were reported by Ashe,⁴⁵ who found that the injection of a thymic extract, "thymocrescine," had an accelerating influence on the growth rate of first generation rats. In later papers from his laboratory, the purification of this substance is reported^{44 46 47 48, 49} and as little as 1 mg injected per day was found to be effective. The active substance contains peptides, amino-acids and sulphur—possibly as cysteine, cystine or glutathione.

The most striking results by this approach have been reported by Rowntree and his collaborators^{50, 51 56 57}. Multiple injections of a dilute HCl extract of calf thymus (Hanson extract) into successive generations of rats causes a striking precocity which is first observed as early as the second generation, and is cumulative through several succeeding generations. Only the early growth period is effected, and the effect is lost upon interruption of the injections during any given generation. Only the females need be in-

jected⁵² "Hanson extract" also contains reduced sulphur compounds and ascorbic acid, and Rowntree's⁵³ group has recently reported that some but not all of the effects of thymus extract may be obtained by injecting cysteine and glutathione and ascorbic acid⁵²

In a brief report, Adler²³ has stated that thymus extract (preparation not described) injected into dogs produces a syndrome resembling myasthenia gravis. He further states that the weakness and collapse exhibited by these animals is immediately abolished by the injection of prostigmin—a striking support for the contention that the condition is myasthenic in nature. Full details of these experiments have not as yet been published.

(4) *Implantation of Thymic Tissue*—Multiple implants of thymic tissue into successive generations of rats seem to have the same effect, but to a less degree, as multiple injections of thymus extract into successive generations^{58, 59}. By repeated transplantation of young thymic tissue into dogs, Adler states that the same myasthenic condition is produced as by injection of thymic extracts²³.

As has been stated, it is difficult to evaluate the effects of therapeutic procedures in myasthenia gravis because of the presence of a tendency to spontaneous remissions. Kennedy and Moersch⁶⁰ report 87 patients with myasthenia gravis observed at the Mayo Clinic between 1915 and 1932. Of the 84 patients whose subsequent course could be traced, 34 were dead at the time of the report (1937). In 24 of these, death was attributed to myasthenia gravis. Of the remaining 50 patients, 13 reported their condition unchanged, ten were improved, and eight were worse. The condition of seven patients had fluctuated greatly, and the answer to the questionnaire was unintelligible in 13 instances. Regarding remissions, Kennedy and Moersch state "In 44 of the cases, no mention was made of a remission, and in three other cases the patients failed to reply to the questionnaires. Twenty-seven patients had 43 complete remissions, which ranged from more than one month to 15 years in duration. The average duration of a complete remission was two and two-tenths years, the majority of them lasted less than one year. Thirteen patients had 17 partial remissions which lasted from less than one to 16 years, the average duration being one and five-tenths years. The majority of these remissions lasted less than six months." Other citations from the literature would only serve to substantiate the point that the course of patients with myasthenia gravis varies greatly. It is generally believed that remissions become shorter in duration as the disease advances. If this is true, it lends greater significance to the possible effect of surgical treatment in our patient since she had experienced increasingly severe attacks during the four-year period preceding operation.

The value of roentgenotherapy of the thymic region in myasthenia gravis is open to question. Pierchella⁶¹ reported improvement following irradiation of a patient with hyperplasia of the thymus and myasthenia gravis. Mella⁶² noted improvement in one of his patients following irradiation of the thymus. Keschner and Strauss⁶³ reported disappearance of the shadow in the mediastinum and a remission in the symptoms following roentgenotherapy. Hyland⁶⁴

noted improvement in two of four patients with myasthenia but without demonstrable thymic lesions following irradiation of the thymic region. On the other hand, some observers have noted no improvement following roentgenotherapy. It is difficult to evaluate the effect of irradiation in our patient. It is known that thymic tumors usually are sensitive to irradiation. The degenerative changes which were present in the tumor in our case strongly suggest that the lesion was affected by roentgenotherapy.

It is our impression that our patient would have died during the severe exacerbation of the disease in the early part of 1936, had prostigmin not been available. As has been stated, operation was postponed until a remission occurred. It is likely that the beneficial effects produced by prostigmin will greatly decrease the dangers associated with surgical operations on individuals with myasthenia gravis. If it is decided in the future that surgical exploration of the thymic region is indicated in patients with this disease, it should be performed through an approach which gives adequate exposure, such as division of the upper part of the sternum. One should not rely upon the imperfect view which is obtained through an incision in the lower part of the neck.

In concluding, we wish to emphasize again the absence of conclusive proof that the improvement noted in our patient is due to the removal of the tumor from the thymic region. It is well known that hypertrophy of the thymus may occur without an associated myasthenic state. It will be necessary to have additional clinical tests before this form of therapy can be accurately evaluated. It is possible that additional experience will show that exploration of the thymic region is indicated in all patients with severe myasthenia gravis. This is particularly apt to be true in those patients with tumors that are not sensitive to irradiation.

SUMMARY

Fifty-three proven instances of myasthenia gravis associated with abnormalities of the thymus have been collected from the literature. This represents approximately one-half of the cases of myasthenia gravis in which postmortem examinations or the findings at operation have been reported. The removal of a tumor from the thymic region of a patient with myasthenia gravis is described. The greatly improved status of the patient during the three years since operation is recorded. This experience may indicate the advisability of the surgical removal of clinically demonstrable thymic tumors in patients with myasthenia gravis.

BIBLIOGRAPHY

- ¹ Ewing, James. *Neoplastic Diseases*. 3rd Ed., W. B. Saunders, 1928, pp. 966.
- ² Buzzard, E. F. *Brain*, 28, 438, 1905.
- ³ Weigert, Carl. *Neurol. Centralbl.*, 20, 597, 1901.
- ⁴ Bell, E. T. *Jour. Nerv. and Ment. Dis.*, 45, 130, 1917.
- ⁵ Norris, E. H. *Am. Jour. Cancer*, 27, 421, 1936.
- ⁶ Minot, A. S., Dodd, K., and Riven, S. S. *Science*, 87, 348, 1938.
- ⁷ Walker, M. B. *Lancet*, 1, 1200, 1934.
- ⁸ Decker, H. R. *Jour. Thoracic Surg.*, 4, 445, 1935.
- ⁹ Crosby, E. H. *Am. Jour. Cancer*, 16, 461, 1932.

- ¹⁰ Froboese-Thiele, F, and Leschcziner, H *Ztschr f klin Med*, **86**, 391, 1918.
- ¹¹ Pulay, Erwin *Neurol Centralbl*, **38**, 263, 1919
- ¹² Mott, F W, and Barrada, Y A *Brain*, **46**, 237, 1923
- ¹³ Auerbach, L *Ztschr f klin Med*, **114**, 388, 1930
- ¹⁴ Halpern, F, and Popper, H *Ztsch f d ges Neurol u Psych*, **132**, 296, 1931
- ¹⁵ Lowenthal, K Quoted by Norris²²
- ¹⁶ Symmers, D *ANNALS OF SURGERY*, **95**, 544, 1932
- ¹⁷ Zajewloschin, M N *Ztsch f d ges Neurol u Psych*, **148**, 28, 1933
- ¹⁸ Gold, E *Wien klin Wchnschr*, **48**, 694, 1935
- ¹⁹ Butt, H R *Arch Path*, **21**, 27, 1936
- ²⁰ Alajouanine, T, Hornet, T, Thurel, R, and Andre, R *Rev Neurol*, **65**, 559, 1936
- ²¹ Alajouanine, T, Hornet, T, and Morax, P *Rev Neurol*, **68**, 871, 1937
- ²² Norris, E H *Am Jour Cancer*, **30**, 308, 1937
- ²³ Adler, H *Arch Klin Chir*, **189**, 529, 1937
- ²⁴ Obiditsch, R A *Virch Arch Path Anat u Physiol*, **300**, 319, 1937
- ²⁵ Peer, G F, and Farinacci, C J *Military Surgeon*, **82**, 350, 1938
- ²⁶ Holmes and Greenfield Discussion of Paper of Mott and Barrada¹²
- ²⁷ Lievre, J A *Presse Méd*, **44**, 991, 1936
- ²⁸ Andrus, W DeWitt, and Foot, N C *Jour Thoracic Surg*, **6**, 648, 1937
- ²⁹ Brem, J, and Wechsler, H F *Arch Int Med*, **54**, 901, 1934
- ³⁰ Meggendorfer, F Quoted by Bell⁴
- ³¹ Schumacher and Roth *Mitt a d Grenzgeb d Med u Chir*, **25**, 746, 1913
- ³² Haberer, H *Arch f klin Chir*, **109**, 193, 1917
- ³³ Riven, S S, and Mason, M F *Southern Med Jour*, **30**, 181, 1937
- ³⁴ Restelli, A *Ticini Regu ex typog Fusi et soci*, 46 pp, 7 pl, 4°, 1845
- ³⁵ Basch, K *Jahrb f Kinderh*, **64**, 285, 1906
- ³⁶ Klose, H, and Vogt, H *Beitr z klin Chir*, **69**, 1, 1919
- ³⁷ Matti, H *Mitt a d Grenzgeb d Med u Chir*, **24**, 665, 1911
- ³⁸ Park, E A, and McClure, R D *Am Jour Dis Child*, **18**, 317, 1919
- ³⁹ Andersen, D *Physiol Rev*, **12**, 1, 1932
- ⁴⁰ Shay, H, Gershon-Cohen, J, Fels, S S, Meranze, D R, and Meranze, T *J A M A*, **112**, 290, 1939
- ⁴¹ Einhorn, N H, and Rowntree, L G *Endocrinology*, **20**, 342, 1936
- ⁴² Einhorn, N H, and Rowntree, L G *Endocrinology*, **21**, 659, 1937
- ⁴³ Gudernatsch, F *Med Rec*, **146**, 101, 1937
- ⁴⁴ Ratti, P *Biochem Ztschr*, **223**, 100, 1930
- ⁴⁵ Asher, L *Endokrinologie*, **7**, 321, 1930
- ⁴⁶ Stotzer, P *Biochem Ztschr*, **234**, 1, 1931
- ⁴⁷ Zenklusen, A *Biochem Ztschr*, **252**, 309, 1932
- ⁴⁸ Nowinski, V W *Biochem Ztschr*, **249**, 421, 1932
- ⁴⁹ Asher, D *Biochem Ztschr*, **257**, 209, 1933
- ⁵⁰ Rowntree, L G, Clark, J H, Hanson, A M, and Steinberg, A *J A M A*, **103**, 1425, 1934
- ⁵¹ Rowntree, L G, Clark, J H, and Hanson, A M *Arch Int Med*, **56**, 1, 1935
- ⁵² Rowntree, L G, Steinberg, A, Einhorn, N H, and Schaffer, N K *Endocrinology*, **23**, 584, 1938
- ⁵³ Schaffer, N K, Ziegler, W M, and Rowntree, L G *Endocrinology*, **23**, 593, 1938
- ⁵⁴ Gershon-Cohen, J, Shay, H, Fels, S S, Meranze, T, and Meranze, D *Science*, **87**, 20, 1938
- ⁵⁵ Gershon-Cohen, J, and Shay, H *Am Jour Roentgenol*, **39**, 203, 1938
- ⁵⁶ Rowntree, L G, Clark, J H, Hanson, A M, and Steinberg, A *Trans Assn Am Phys*, **49**, 252, 1934
- ⁵⁷ Rowntree, L G, Clark, J H, Steinberg, A, Einhorn, N H, and Hanson, A M *Trans Assn Am Phys*, **51**, 148, 1936
- ⁵⁸ Einhorn, N H, and Rowntree, L G *Endocrinology*, **22**, 342, 1938

- ⁵⁹ Einhorn, N H Endocrinology, 22, 435, 1938
⁶⁰ Kennedy, F S, and Moersch, F P Canad Med Assoc Jour, 37, 216, 1937
⁶¹ Pierichella, L Therap Halbmonatsh, 35, 504, 1921
⁶² Mella, H M Clin North Amer, 7, 939, November, 1923
⁶³ Keschner, M, and Strauss, I Arch Neurol and Psych, 17, 337, 1927
⁶⁴ Hyland, H H Canad Med Assoc Jour, 35, 372, 1936

DISCUSSION—DR ROY D McCLURE (Detroit, Mich) A gland, to be called a gland, surely should have a secretion either internally or through ducts. A study of the embryologic development of the thymus suggests that it should be classified as a gland because its origin is similar to that of the thyroid and parathyroid. Much work has been done in an effort to prove that the thymus is truly a gland, and there have been many shipwrecks among those who have tried to prove that it has a function.

Doctor Blalock has kindly called attention to the work that Doctor Edwards Park and I had done. This was inspired by the work of the Germans, Kloss and Vogt, who had obtained a picture of rickets in their early thymectomized dogs. Their results, in 1914, seemed so specific and so striking that we were impelled to repeat their work. Others had obtained similar results. Park and I failed to get any effect from careful, complete, early thymectomies in dogs. I remember our talking at the lunch table at Hopkins one day about this subject before two of our German exchange doctors. Our animals, which we kept in free runways in the country with a caretaker, were in excellent shape, you could not tell the difference between the controls and our animals with complete early thymectomy. One of these foreign doctors was the son of a famous German professor of medicine. We were talking of our failure in getting results. He said, "You must go to Germany and see where you make your mistake." It happened that one of our assistants, Dr. Henry Cave, was going to Germany that year and he was very glad to visit Kloss and Vogt. When he came back, he told us of their animals, which were confined in small cages in a dark cellar, and that their diets were inadequate. It was obvious, therefore, that the experimental results which they had obtained were on the basis of diet deficiency.

One day, while I was Resident Surgeon at the Johns Hopkins Hospital, Doctor Halsted, who had authorized and encouraged our experimental work, became (for him) greatly excited over an article published by von Haberer, reporting a series of exophthalmic goiter cases which had not been cured by operation. Von Haberer had recalled one of these cases, and had removed the thymus gland which, as we know, is so greatly enlarged in this disease. That patient got well. Immediately we recalled, for Doctor Halsted, all the cases of exophthalmus which had not recovered. They were all given iodine-therapy and some of them had a partial thymectomy. I believe none of them were much benefited, to our great disappointment.

Then along came the work of Doctor Rowntree, and his amazing growth-results in the second and third generations of rats. We followed his work with great interest, because it looked as if, at last, he had found an internal secretion of the thymus. But now, even he admits that this result is due perhaps not to the thymus gland but to glutathione, which has a very high content of amino-acid with sulphur (that is cystine and glycine), for by feeding glutathione he can get the same results that he obtained by feeding thymus. The problem, therefore, appears to be far from being solved.

This report of Doctor Blalock's is so striking that time and further similar cases can alone clear this up. We have had ten cases of thymic tumor at the Henry Ford Hospital, but none of them associated with myasthenia gravis. However, it certainly behooves us all to look up our cases, both of myasthenia

gravis and of tumors of the thymus, and see if we can possibly help to clear up this subject

DR GEORGE J HEUER (New York) Doctor Blalock, again, has raised the interesting question of the relationship between myasthenia gravis and pathologic conditions of the thymus gland. His patient, whom we have had the opportunity of seeing, supports the view that there exists a relationship between myasthenia gravis and certain tumors of the thymus. My own interest in the matter dates back many years, when I had the opportunity of studying, on Doctor Halsted's service, a patient with marked exophthalmic goiter who also had symptoms and signs of myasthenia gravis. It was at a time when, particularly abroad, the relationship between the thyroid and thymus in exophthalmic goiter was being emphasized and we were inclined to attribute the manifestations of myasthenia gravis to disease of the thymus gland. About 1930, I collected all the malignant tumors of the thymus gland reported in the literature, finding at that time 85 to 90 cases. I did not find any cases of malignant tumor of the thymus gland in which myasthenia gravis was stated to have been present, but it should be said that in many of the reports specific comments on the presence or absence of this condition are not made.

Dr N C Foot, in his own experience, and in his survey of the literature, failed to find an association between malignant tumors of the thymus and myasthenia gravis. On the other hand, necropsies in patients dying with myasthenia gravis have shown, in about 50 per cent of the cases, a benign enlargement of the thymus, according to descriptions given, a benign hyperplasia, a circumscribed benign tumor or a diffuse benign tumor. As between the circumscribed enucleable tumors and the diffuse tumors, it is my impression that it has been in the former, as in Doctor Blalock's case, that myasthenia gravis has been particularly associated. It is possible, although not yet established, that a particular type of thymic tumor is associated with myasthenia gravis. All cases of thymic enlargement associated with myasthenia gravis should, therefore, be most carefully studied in the hope of clarifying what is now an obscure relationship.

DR PETER HEINBECKER (St Louis) I am glad that Doctor Blalock stressed the fact that myasthenia gravis is a disease which is characterized by exacerbation and remissions. These exacerbations and remissions are especially likely to occur at the time of puberty or during pregnancy. They may be precipitated by almost any cause. Also, they are not infrequently of long duration.

Now, as to the underlying mechanism in myasthenia gravis, I am doubtful that it is a weakness of the myoneural junction. I think it is an inability of the muscle to build up quickly the state or materials necessary for a muscular contraction. This statement is based on an examination I made a couple of years ago in a case of myasthenia gravis. I carried out a nerve muscle biopsy and stimulated the nerve about 100 times a second, observing its activity for two hours with a cathode ray oscillograph. It acted in a perfectly normal manner. I stimulated the excised muscle with an electrical current. The first responses were normal and then gradually fatigue set in. If the muscle was allowed to rest, it again contracted normally, soon once more to fatigue. When one stimulates the muscle directly with an electrical current it is not necessary to assume the participation of the myoneural junction in the excitatory process. The contractile process of the muscle is defective. I do not believe that any experimental evidence has indicated that an excess of thymus hormone interferes with the processes of muscular contraction.

LEFT SUBPHRENIC ABSCESS*

BURR N CARTER, M D

CINCINNATI, OHIO

FROM THE DEPARTMENT OF SURGERY OF THE COLLEGE OF MEDICINE, UNIVERSITY OF CINCINNATI, AND THE CINCINNATI GENERAL HOSPITAL, CINCINNATI, OHIO

MUCH has been written on the subject of subphrenic abscess and many excellent articles are available dealing with the difficulties of its differential diagnosis, its high mortality and the various methods of drainage of such abscesses. Throughout such articles one finds, however, little on the subject of the *left* subphrenic abscess, all of the emphasis being placed on those which occur on the right side. This is due, in all probability, to the fact that subphrenic abscess occurs more frequently on the right side, for example Ochsner,¹ in reviewing 1,517 cases of subphrenic abscess, found that only 412 were on the left, or one abscess on the left to three on the right. Table I, based on some of the more recent literature, indicates that the ratio is about three abscesses on the right side to one on the left. In spite of the fact that subphrenic abscesses occur once on the left for every three or four times on the right, the occurrence of a left subphrenic abscess is not often thought of when the surgeon considers the possibility of a subphrenic abscess in a given case. He is quite apt to feel, after he has ruled out the presence of pus beneath the right half of the diaphragm, that he can entirely dismiss from his consideration the presence of a subphrenic abscess. The old adage "pus somewhere, pus nowhere, pus under the diaphragm" is certainly an excellent one, but should be modified to "pus somewhere, pus nowhere, pus not under the right half of the diaphragm, pus under the left half of the diaphragm." It is frequently stated, and rightly so, that one of the most important aids in making a correct diagnosis of subphrenic abscess is first of all to bear in mind its possible occurrence. The diagnosis is missed or long delayed in practically all abscesses occurring beneath the left half of the diaphragm because, though the occurrence of a subphrenic abscess is considered, its possible location on the left side is rarely kept in mind. To most surgeons "subphrenic abscess" really means "right subphrenic abscess."

Anatomy—In 1908, Barnard² gave a very accurate description of the anatomy of the subdiaphragmatic space, and his splendid article is referred to by nearly all of the subsequent writers on the subject of subphrenic abscess. Recently Alton Ochsner has given an excellent description of this area, also, which is a modification of Barnard's. Three subdiaphragmatic spaces on the left side were described by Barnard and it is proposed to follow his terminology in this communication. The spaces are (1) The left anterior intraperitoneal, (2) the left posterior intraperitoneal, and (3) the left extraperitoneal. The *left anterior intraperitoneal space*, which is likewise

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12,

LEFT SUBPHRENIC ABSCESS

TABLE I

ANALYSES OF SUBPHRENIC ABSCESSES PREVIOUSLY REPORTED

Author	Total Cases Reported	Number on the Left Side	Location of Left-Sided Abscesses		
			Anterior Intraperitoneal	Posterior Intraperitoneal	Extra-peritoneal
Ochsner and Graves ¹ (own series)	50	5	5	0	0
Overholt ¹⁰	25	2	2	0	0
Schwartz ⁴	9	2	2		
Fisfield and Love ⁸	78	22	14	7	1
McNamee ¹⁶	9	3	3		
Pancoast ¹⁹	16	3	2		1
Gatewood ⁶	41	9	Not localized as to space		
Barnard ²	83	33	30	3	
Gogol ⁹	50	0	0	0	0
Beye ⁵	23	6	Not localized as to space		
Delario ¹⁸	7	1	1		
Lockwood ³	82	23	12	8	3
Totals	473	109	71	18	5

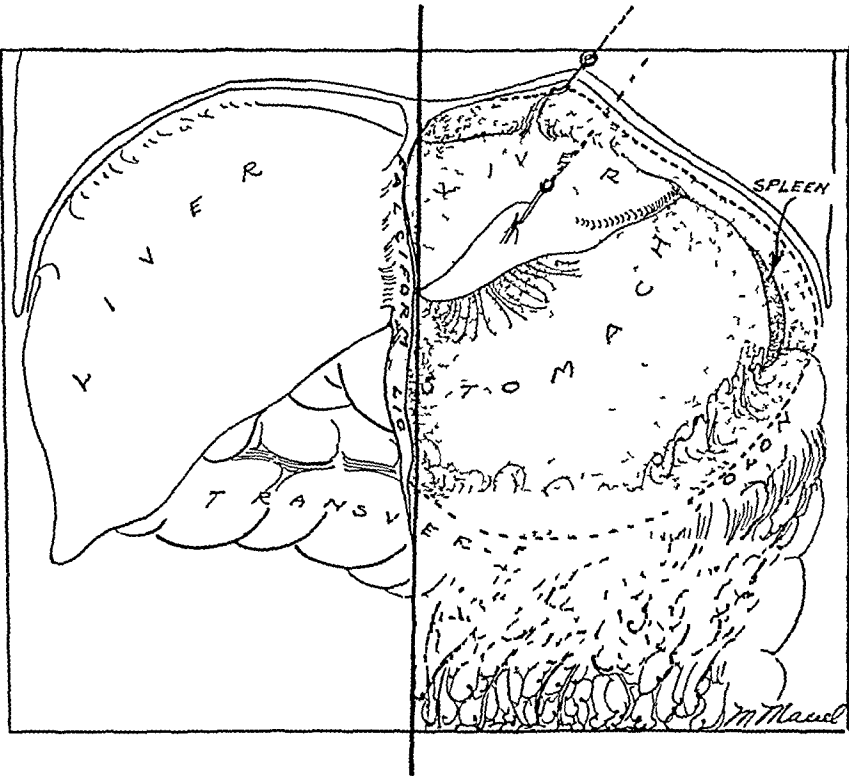


FIG 1—The anatomy of left anterior intraperitoneal abscess. The abscess is represented by the dotted area. The transverse colon adherent to the anterior abdominal wall is shown limiting the abscess below.

called the perigastric or perisplenic space, has the following boundaries. The diaphragm above, the left lobe of the liver below and to the right, the spleen to the left, the coronary and falciform ligaments to the right, the left lateral ligament behind and the adhesions between the stomach or the omentum to

the anterior abdominal wall below (Figs 1, 2 and 3) Although the boundaries of the entire left anterior intraperitoneal space are those just given, the abscess occupying it may not extend to these limits, but may be localized to smaller areas by the formation of adhesions within the space For instance,



FIG 2—The anatomy of a left anterior intraperitoneal subphrenic abscess in the parasternal line. A normal section is shown on the left. Note that the left lateral ligament of the liver forms the posterior boundary of the abscess at this level. The stomach by adhering to the anterior abdominal wall has limited the abscess below so that the abscess barely presents below the costal margin.

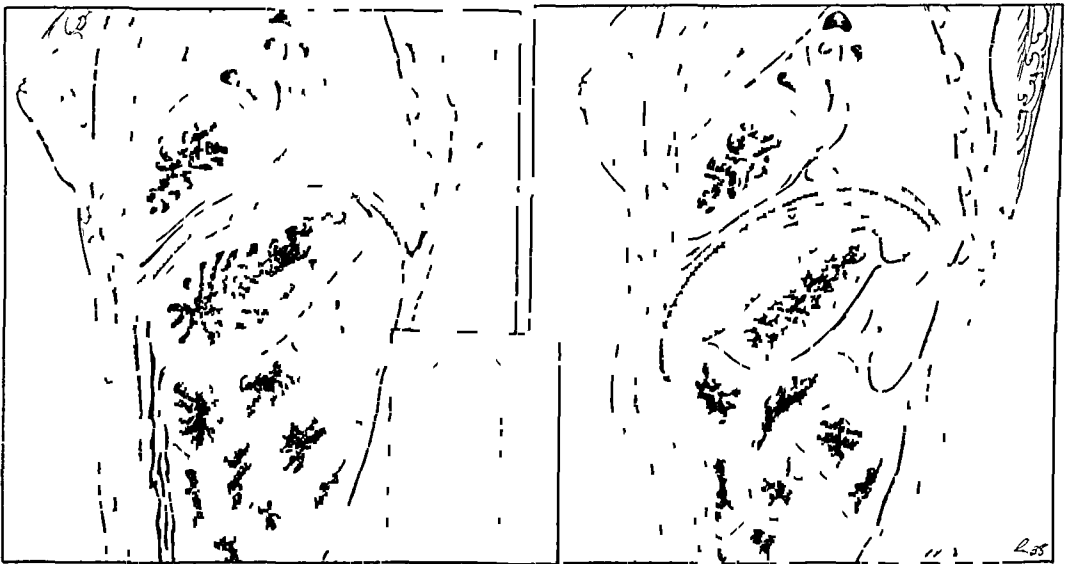


FIG 3—The anatomy of a left anterior intraperitoneal subphrenic abscess in the nipple line. A normal section is shown on the left. At this level the spleen limits the abscess behind and somewhat laterally. The omentum has become adherent to the abdominal wall below and forms the lower boundary of the abscess so that a considerable portion of the abscess presents below the costal margin. (Cf Fig 2)

the stomach may adhere to the abdominal wall just at the costal margin and limit the abscess anteriorly (Fig 2). Whereas, if the colon or mesocolon forms the lower boundary, the abscess will present as a mass in the left upper quadrant (Fig 3)

LEFT SUBPHRENIC ABSCESS

The left anterior intraperitoneal space has connections with other spaces and pouches which are important from the point of view of spread of infection from elsewhere *to* this space and spread of pus *from* it to other areas. It connects around the left margin of the liver with the right subhepatic space and below with the left lumbar pouch which lies between the descending colon and the lateral abdominal wall. Barnard described a direct pathway from the pelvis to the left anterior intraperitoneal space (Fig 4) of which I have found no other mention made, but which is of importance, for it explains why a left subphrenic abscess so frequently follows suppuration in the pelvis.

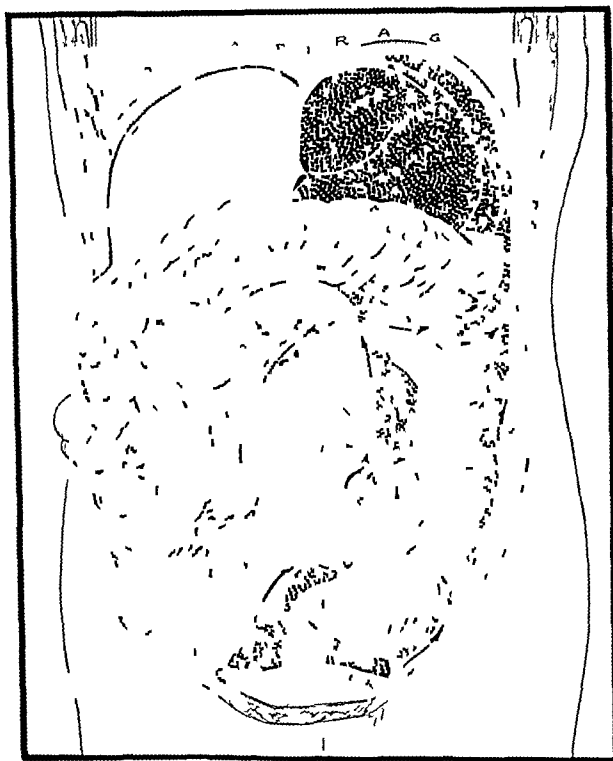


FIG 4—The pathways by which pus spreads from the pelvis to the left subphrenic space. The lumbar pouch is shown to the outside of the descending colon and the route described by Barnard² to the inside, with the spine forming the medial boundary up to the duodenojejunal flexure at which point the pus is directed around the left edge of the splenic flexure into the left anterior intraperitoneal space.

This pathway leads from the rectovesical or recto-uterine pouch over the left sacro-iliac joint to the gutter formed by the vertebral column on the right, the descending colon on the left and the mesentery behind. This gutter directs the pus up to the duodenaljejunal flexure whence it passes forward along the splenic flexure to reach the left anterior intraperitoneal subphrenic space. Barnard states that a "trail of pus" can be found along this route in many cases of pelvic peritonitis. Pus may also reach the left subphrenic space from the pelvis by flowing along the left lumbar pouch, *i.e.*, between the colon medially and the lateral abdominal wall laterally (Fig 4). With the patient in a recumbent position, it can readily be seen how pus could spill out of the pelvis and be directed by one of these two routes to the left subphrenic space. In five of the six cases herewith reported, there was pus in

the pelvis before the development of a left subphrenic abscess, namely, three cases of postpartum infection, one of a localized pelvic abscess ("which disappeared suddenly") and one of a pelvic appendix which had ruptured, filling the true pelvis with thick pus

The *left posterior intraperitoneal space* is in reality the lesser peritoneal sac. This space is primarily infected by the perforation of a gastric ulcer or carcinoma situated on the posterior aspect of the stomach. It may be secondarily infected by pus entering the foramen of Winslow, usually from a right subhepatic abscess.

The *left extraperitoneal space* is the loose areolar tissue which surrounds

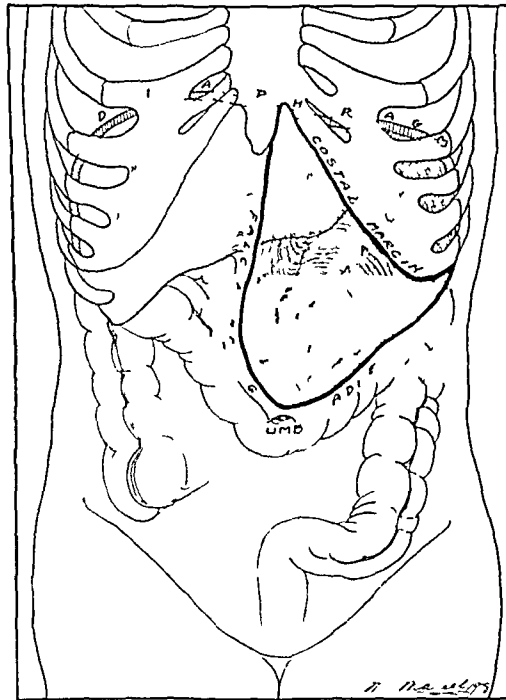


FIG 5—The triangular area of fulness and tenderness which is present in the type of large left subphrenic abscess when the transverse colon forms the lower limit of the abscess, and the falciform ligament the right boundary

the kidney, the pancreas and the descending colon on its posterior aspect. It is very rarely infected. Cases of abscess in this area have been reported by Barnard as following an infection of the vertebral bodies, a long standing chronic empyema and a stomach ulcer which had perforated posteriorly. Clinically, such abscesses point in the lumbar region and simulate the perirenal abscesses.

Of the three spaces described, the most important is the *left anterior intraperitoneal*, chiefly because it is the most frequently infected.

Signs and Symptoms—The diagnosis by physical examination of an abscess beneath the left leaf of the diaphragm is even more difficult than it is when the abscess lies beneath the right half of the diaphragm, for such an abscess gives fewer physical signs of its presence. On the right, the firm,

large right lobe of the liver forms the floor of the abscess, whereas, on the left, there is little liver substance, but the abscess is encompassed below by more yielding structures, such as stomach, falciform ligament, colon, spleen and transverse mesocolon. Consequently, on the left there is apt to be less bulging in the lower thorax and costal margin, less restriction of movement of the lower portion of the thoracic cage, less local pain because of less tension of the pus and less elevation and fixation of the diaphragm itself. It is true, however, that in the case of the left anterior intraperitoneal abscess (most common variety) tenderness on pressure beneath the costal margin can be elicited earlier and more definitely than on the right, and when it reaches a large size it may actually be felt as an indefinite mass below the left costal margin. If the whole space is filled with pus one can outline a characteristic triangular mass described by Barnard as extending from under

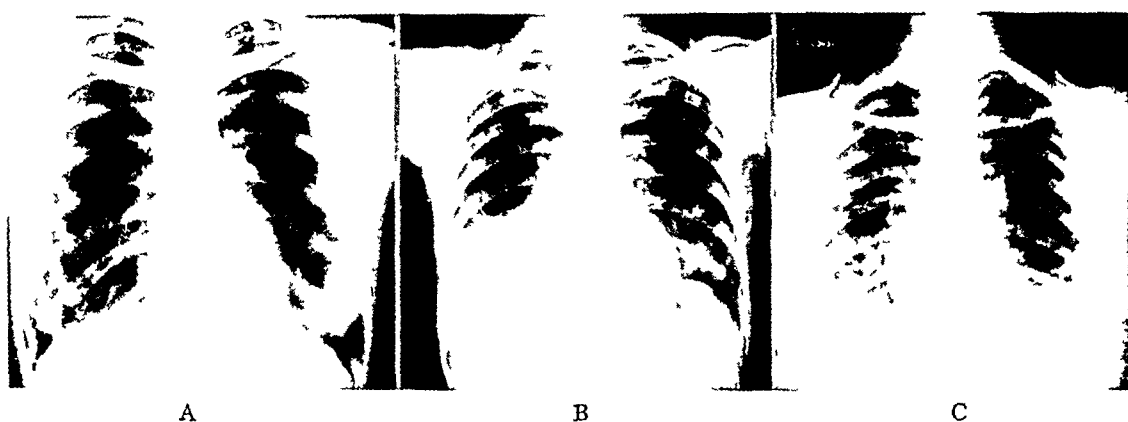


FIG 6—(A) Normal relationship between the right and left halves of the diaphragm. (B) The relationship between the two halves of the diaphragm in a case of right subphrenic abscess. The elevation of the right half of the diaphragm is very evident. (C) The relationship between the right and left halves of the diaphragm in a case of left subphrenic abscess. The elevation of the left half of the diaphragm is scarcely noticeable.

the left costal margin to a line from umbilicus to costal margin and from ensiform cartilage to umbilicus (Fig 5). Pain referred to the shoulder and neck is greater with left-sided abscesses because of the less fixed diaphragm, the movement of which against the abscess causes the pain to be referred to the neck. In five of the six cases reported herewith, severe pain in the left lower thorax and in the neck was a prominent symptom. Owing to the fact that the abscesses which occur on the left side are apt to be diagnosed late, the so-called "thoracic signs" are more commonly seen than in the case of right-sided abscess. These signs are "fuzziness" of the diaphragm on the roentgenogram, those of pneumonitis, or those of fluid (serous or purulent) of varying amount in the pleural cavity. In fact, it is only too often the signs of fluid in the left pleural cavity, which is secondary to the abscess, that bring about the diagnosis of the abscess itself. Such was the case in two instances in the series reported here. It is most essential to bear in mind that fluid above the diaphragm frequently means pus below it and to suspect the abdomen rather than the chest.

Roentgenologic and Fluoroscopic Examination—The roentgenogram and

the fluoroscope are probably the most useful aids in establishing a diagnosis of subphrenic abscess. Examination under the fluoroscope characteristically shows a high, fixed diaphragm in the case of right-sided abscess. With the left-sided abscess, however, the diaphragm is not so high for the reasons given above. Even if it is high, the discrepancy of its height as compared to that on the right is not so noticeable, since it normally is lower than the right, or its elevation may be attributed to abdominal or gastric distention, both of which influence the left half of the diaphragm more than the right (Fig 6). On the left, however, fixation of the diaphragm is a most important sign of an abscess beneath it, and it occurs even though the diaphragm is not high. The presence on a roentgenogram of an air bubble beneath the right half of

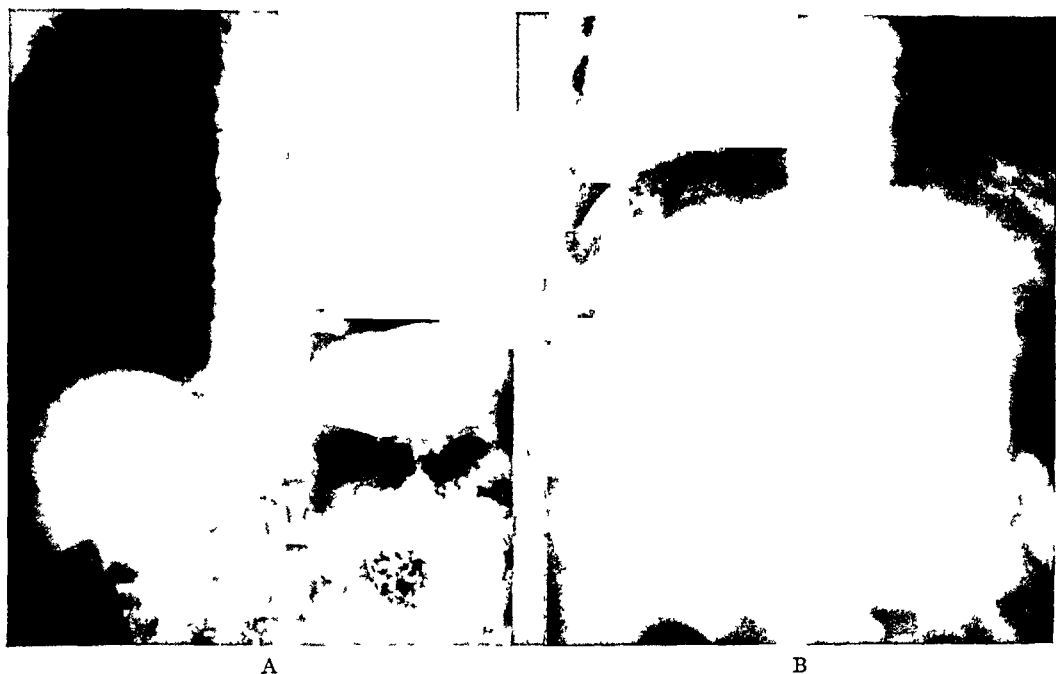


FIG 7—Roentgenograms showing (A) the normal relationship of the barium filled stomach to the diaphragm, and (B) the downward and medial displacement of the stomach by the subphrenic abscess in Case 4.

the diaphragm with a fluid level beneath it clinches the diagnosis of subphrenic abscess. This finding is said to occur in from one-fourth to one-half of the cases of subphrenic abscess and can be detected if films are taken from various angles. Air and fluid beneath the right half of the diaphragm are easy to detect, but beneath the left half, confusion is caused by the normal findings of air and fluid in the stomach. Consequently, the fluid level and air in a subphrenic abscess are easily overlooked on the left side. The true nature of such an air can be very easily determined by the simple expedient of filling the stomach with barium. Normally the stomach, when filled with barium and with the patient in a low Trendelenburg position, lies in contact with the diaphragm (Figs 7 and 8). If there is an abscess beneath the diaphragm, the barium-filled stomach will be found to be separated from the undersurface of the diaphragm by a considerable space which may contain air or may not. Even if there is no air in a left subdiaphragmatic abscess, the filling of the

stomach with barium will establish the diagnosis, owing to the displacement of the stomach downward and medially and posteriorly by the abscess if it lies in the anterior space, or anteriorly if the abscess lies in the posterior space (Figs 7 and 8). After being given the barium by mouth, the patient should be placed in a low Trendelenburg position to insure that the stomach comes in contact with the diaphragm if it is possible for it to do so. By this one simple maneuver, the diagnosis of left subphrenic abscess becomes a much simpler and easier matter, yet I can find no reference to its use in the surgical literature. It should be used whenever there is a suspicion of a left subphrenic abscess.

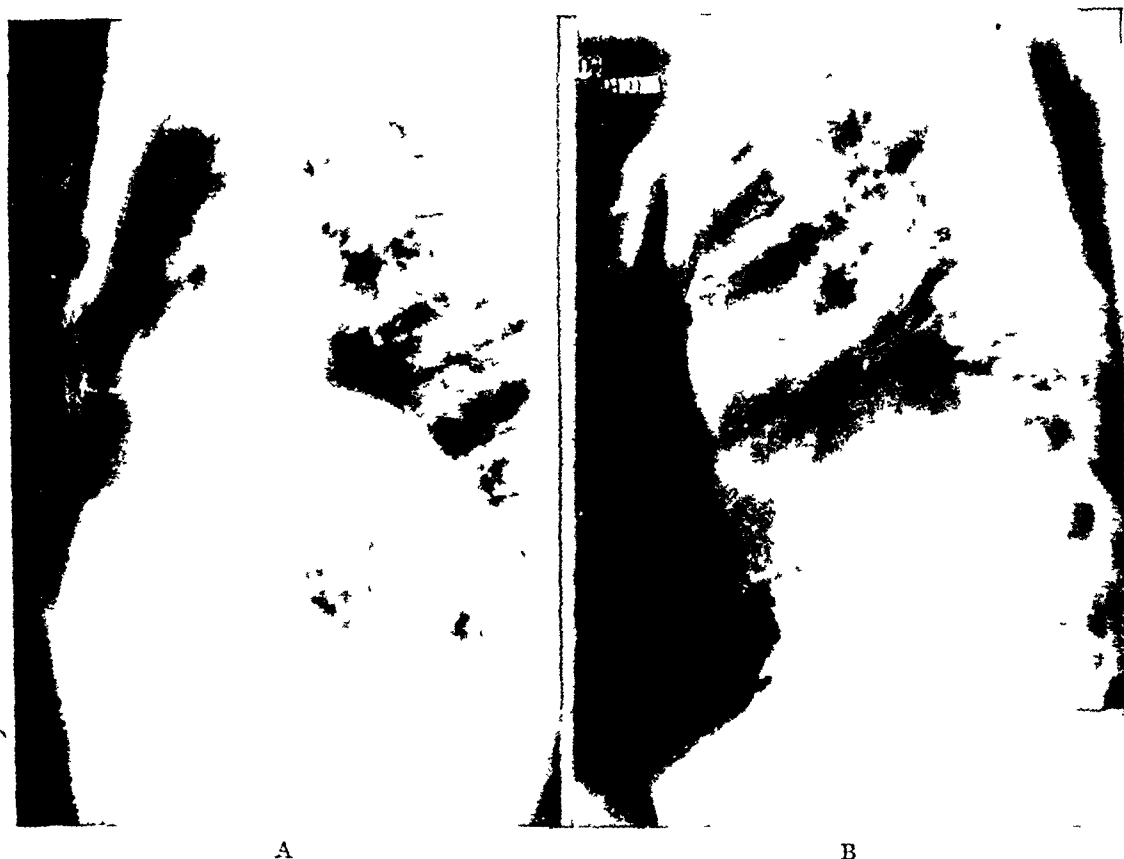


FIG 8—Lateral roentgenograms showing (A) the normal relationship of stomach to diaphragm, and (B) the downward displacement of the stomach by the subphrenic abscess in Case 4.

CASE REPORTS

Case 1—Hosp, No 5758G F L, female, age 19, was admitted to the Good Samaritan Hospital, August 21, 1935, complaining of weakness and pain in the left upper quadrant and lumbar region. Her past history was of no importance. Her present illness began in November 1934, when, after having been delivered of a normal child, she contracted a postpartum infection to which she nearly succumbed. She was confined to bed in another hospital from the time of delivery until February 20, 1935. After being at home and in bed for three months she began to be up and about. During this time she ran a low-grade fever, felt weak and sick and had a soreness and pain in her left lower chest and upper abdomen. These symptoms became more acute in August, 1935, when she was admitted to the Good Samaritan Hospital in care of Dr F Williams and Dr Clyde Roof. It was found that she had been having severe knife-like pains in the upper left quadrant and a sharp pain referred to her left shoulder, that there had been occasional attacks of vomiting.

and a feeling of weakness and lassitude. Her temperature ranged between 98° and 100° F, pulse 100, respirations 20. WBC 10,375, RBC 3,700,000, Hb 72 per cent.

Physical Examination—There was lagging of the left costal border with some fulness, dullness at the left base and very little excursion of the diaphragm. Roentgenologic examination of the chest showed a high diaphragm on the left with no fluid in the pleural cavity and the lungs clear. Fluoroscopic examination revealed that the left diaphragm was high and fixed and that there was an air space with a fluid level just beneath the diaphragm. Barium was given by mouth and films taken with the patient lying flat on the table. These showed that the true air bubble in the stomach was separated from the air space referred to above by a considerable distance. From these examinations it was obvious that one was dealing with a left subphrenic abscess. A barium enema was given, and some of the barium was found to enter the abscess cavity. It was clear now that the subphrenic abscess communicated with the transverse colon, having ruptured into it at some previous time.

Operation—September 3, 1935, Doctor Roof. Nitrous oxide-ether anesthesia. Suspecting that there might be difficulty in localizing the abscess, a short, high, left rectus incision was made, and the abscess located beneath the costal margin. A short segment of rib in the midaxillary line was resected. A rubber tube and cigarette drains were inserted. The abscess cavity, which was about 10 cm in diameter, lay between the anterior portion of the diaphragm and the undersurface of the liver above and the transverse colon and spleen below, and was bounded posteriorly by the stomach—in other words, it was a left anterior inferior subphrenic abscess.

The wound drained feces and pus for two weeks and then rapidly healed. The patient was discharged, September 20, 1935. She was readmitted, November 6, 1936, at which time her right tube, ovary and appendix were removed. Since then she has remained well.

COMMENT—The diagnosis in this case was made nine months after the onset of a postpartum infection, which seems to have been the logical cause for the subphrenic abscess. It is impossible from the history to determine when the abscess ruptured into the colon, but from its small size, when found at operation, and from its thick fibrous walls, the rupture must have occurred many weeks before operation. The repeated episodes of fever and malaise which occurred at intervals during her long illness must have been due to periods of poor drainage of the contents of the abscess into the colon. It is interesting that on fluoroscopic examination an air bubble was seen beneath the left diaphragm, but one could not be sure whether the air bubble was in the stomach or not until the barium was given. Barnard reports spontaneous rupture of 23 subphrenic abscesses, occurring into the bronchus in four cases, into the pleura in five cases, into the stomach in eight cases, into the colon in two cases, through the skin in two cases, into the peritoneal cavity in one case and into the small intestine in one case.

Case 2—Hosp No 101749. J. L. E., white, male, age 31, was admitted to Christ Hospital, March 12, 1936, with a diagnosis of "a ruptured appendix with peritonitis." He was operated upon immediately by Dr. E. A. Kindel. Through a McBurney incision, a ruptured gangrenous, pelvic appendix was removed, a colon bacillus and Staphylococcus peritonitis found and cigarette drains were placed into the pelvis and down to the cecum (a large fecalith had been removed from the pelvis). After a stormy convalescence for four days, he began to improve considerably, but ten days after operation, he began to complain of pain in the left lower thoracic region and on examination signs of fluid were detected in the left chest. The left pleural cavity was aspirated, March 24, 1936, 12 days after operation, and 10 cc of yellow, cloudy fluid was obtained, which was negative

LEFT SUBPHRENIC ABSCESS

for organisms on smear and culture. A roentgenogram of the chest, March 27, showed "fluid in the left chest." On April 1, 700 cc of fluid of the same character was removed from the left pleural cavity, and on April 9, 28 days after operation, 600 cc of frank pus with a fecal odor was withdrawn. On the following day, a closed aspiration drainage was established in the left pleural cavity. At this time the patient appeared extremely toxic, slightly jaundiced, the tube in the left chest was functioning well, the abdomen was moderately distended and a large tender mass in the region of the right lobe of the liver was made out.

Operation—April 11, 1936, Doctors Kindel and Carter. There was a good deal of bile-stained fluid in the peritoneal cavity. The right lobe of the liver was very large and bulging, it was opened and an abscess containing about 1,000 cc of bile-stained pus and inspissated bile was evacuated. After removal of the pus, a large cavity remained, which we took to be in the liver, and from which a prolongation extended far up toward the left lobe. The edges of the opening in the liver were sutured to the peritoneum and the rest of the wound loosely closed after soft rubber tubes and cigarette drains had been placed into the abscess cavity.

The abdominal wound drained large quantities of bile-stained pus and bile, and the tube in the left thorax discharged foul-smelling pus. One month after operation, both wounds had ceased to drain, and the patient was discharged. He has remained well since that time. During the convalescence repeated roentgenograms showed a cavity below the diaphragm as well as an empyema cavity above it, so that the diagnosis of left subphrenic abscess was established beyond question.

COMMENT—Ten days after operation, fluid was discovered in the left pleural cavity. This, combined with the pain in the left lower chest, was the first evidence of the left subphrenic abscess and it is probable that the abscess could have been diagnosed at that time had barium been given by mouth and roentgenograms taken with the patient flat on the table or in a slight Trendelenburg position. It is interesting to speculate as to whether the liver abscess was the cause of the left subphrenic abscess, due to its rupturing under the diaphragm, or whether the subphrenic abscess burrowed into the liver as well as through the diaphragm and then caused the liver abscess. The anatomic location of the subphrenic abscess was not definitely determined.

Case 3—Hosp No 79071. F. J., colored, male, age 14, was admitted to the Cincinnati General Hospital, August 28, 1937, with a diagnosis of ruptured appendicitis. He was immediately operated upon, and a gangrenous, ruptured appendix removed. A good deal of odorless, thick fluid was aspirated from the peritoneal cavity and the peritoneum closed tightly, only the wound itself being drained. Six days after operation, a small pelvic abscess was detected, which increased in size until the tenth day, when it suddenly disappeared. Coincident with its disappearance, the patient became acutely ill, with a distended abdomen, high temperature and vomiting, it was felt that the pelvic abscess had ruptured into the peritoneal cavity. Under appropriate treatment the peritonitis subsided within two or three days. On the fourteenth day after operation, the patient complained of pain in the left lower chest—there were signs of fluid in the left chest, both on physical examination and roentgenologically. An aspiration of the left chest was productive of cloudy, straw-colored fluid, which contained a few Cocci and Bacilli. This fluid became frankly purulent within two days, and a closed drainage was established in the left pleural cavity. The tube did not function well on account of the thickness of the pus, so, on September 28, 1937, a four-inch segment of the eighth rib in the midaxillary line was resected and a wide opening made into the empyema cavity. It was immediately obvious that there was a hole through the diaphragm leading into a left subphrenic abscess. Up until this time, there had been no mention made of the possibility of such

an abscess being present. The opening in the diaphragm was enlarged by excising a portion of it. A large, soft rubber tube was placed in the cavity and the wound left open. Lipiodol was injected into the sinus and the subphrenic abscess well demonstrated, it was a *left anterior intra-peritoneal* abscess. This patient developed a large pelvic abscess and a large intra-abdominal abscess in the region of the McBurney incision. Both of these were drained and the remainder of the convalescence was smooth, the patient being discharged "well" but rather badly battle scarred, December 1, 1937. He has remained well since.

COMMENT—The diagnosis of a left subphrenic abscess was not made in this case until after an empyema cavity had been widely opened and the opening through the diaphragm actually seen. A "subphrenic abscess" (meaning a right subphrenic abscess) had been thought of and ruled out by repeated fluoroscopic examinations. The diagnosis of left subphrenic abscess was missed because *it was not considered*. Had it been thought of, the correct diagnosis could have been made when the first complaint of pain in the left chest was mentioned.

Case 4—Hosp No 86564. L. J., colored female, age 42, was admitted to the Cincinnati General Hospital, January 27, 1938. She was a very obese woman who was eight months pregnant and was suffering from early antepartum eclampsia. Blood pressure 226/150. She was dyspneic, had edema of the lower half of her body, and a temperature ranging up to 103° F. Her membranes ruptured spontaneously and after the introduction of a Braun bag she was delivered of a macerated fetus by version and extraction, the placenta being removed manually. Following delivery, she developed a puerperal sepsis with signs of peritonitis and nonhemolytic Streptococci in her blood stream. Large doses of sulfamidamide were given together with two transfusions. The blood culture became negative, the blood pressure fell to 120/70 and the peritonitis subsided. One month after admission, she was running a temperature up to 100.4° F, the abdomen was soft and not tender. An abscess of the buttock was drained, March 1, and the temperature fell to 99° F. On March 10, she began to complain of sharp, cutting pains in the lower left chest. The pain continued, increased in severity, and she began to have sharp pains on inspiration referred to her left shoulder.

Diaphragmatic pleurisy was suspected, and a fluoroscopic examination was made, March 12. This revealed a fixed diaphragm on the left, the two crura being on the same level. On March 18, the patient had a severe chill and the temperature rose to 103° F. On March 24, she vomited several times, complained of generalized abdominal pains, became distended and had generalized tenderness over the whole abdomen. She was seen by the Surgical Service, March 24. At that time, there were signs of a generalized peritonitis and a suggestive mass could be felt below the left costal margin. A diagnosis was made of left subphrenic abscess with rupture and resulting peritonitis. Fluoroscopic examination on that day showed the left diaphragm to be fixed and to be "slightly" elevated. A roentgenogram, made after a barium meal, showed the *fundus of the stomach displaced downward and medially*.

Operation—Under local anesthesia, a four-inch segment of the ninth rib was resected in the left midaxillary line. The parietal pleura was edematous and firmly adherent to the diaphragm, the diaphragm was, therefore, opened widely and an abscess containing about 200 cc of thin, foul pus was found beneath it. The abscess lay anteriorly and extended forward to the costal margin and laterally to the spleen. It was an *anterior intra-peritoneal subphrenic* abscess. Two large, soft rubber tubes were inserted and the wound left open. Her postoperative course was stormy. The signs of peritonitis continued and a mass appeared in the upper right quadrant. On April 9, an incision was made over this mass and 120 cc of thin, foul pus evacuated. Pus was seen to well up

LEFT SUBPHRENIC ABSCESS

from between loops of bowel near the collection of pus noted above. The patient died seven hours after the operation. No autopsy could be obtained.

COMMENT—The symptoms of pain in the lower left chest and pain referred to the left neck and shoulder appeared six weeks after the postpartum infection, and at that time a fluoroscopic examination was made. It is significant that though the report stated that the left diaphragm was fixed and on the same level as the right, it made little impression on the attending physicians. If the right diaphragm had been correspondingly as high as the left really was, I venture to say that the diagnosis of right subphrenic abscess would have been made at once. The correct diagnosis was made by the single expedient of a barium meal followed by a roentgenogram taken in a slight Trendelenburg position, but only after the abscess had ruptured with the production of a fatal peritonitis.

Case 5—Hosp. No. 93036. E. T., white, male, age 53, was admitted to the Cincinnati General Hospital, April 15, 1938, one and one-half hours after having been stabbed in the abdomen. He was in mild shock, quite drunk, and difficult to manage. There were two stab wounds through the abdominal wall, one below and to the right of the umbilicus, and one at the outer edge of the left rectus muscle just below the costal margin. He persisted in refusing to be operated upon throughout his stay in the hospital. He was treated with a continuous Wangenstein drainage, a blood transfusion of 300 cc daily for eight days, morphia, and was placed in Fowler's position. He lived for ten days, and died with all the signs of sepsis and peritonitis. On the fifth day of his illness, he began to show some dulness at the left base with limitation of the movements of the left half of the diaphragm. A fluoroscopic examination, made on the eighth day, showed a fixed, high diaphragm on the left, but no barium was given by mouth on account of the patient's abdominal condition. An autopsy was obtained.

Autopsy—There was an old generalized peritonitis, fibrinous in character, two ragged holes in the ileum, which were sealed-off against the anterior abdominal wall, and an abscess holding 500 cc of pus beneath the left diaphragm. This abscess was bounded by the diaphragm above, by the right lobe of the liver and stomach medially and inferiorly by the spleen and transverse colon.

COMMENT—The correct diagnosis of left subphrenic abscess was advanced in this case, and was based upon pain in the left lower chest, limitation of motion of the left costal margin, and a fluoroscopic finding of a high, fixed diaphragm. Barium could not be given by mouth due to the perforation in the intestine.

Case 6—Hosp. No. 99578. A. B., white, female, age 29, was admitted to the Cincinnati General Hospital, July 6, 1938, with a diagnosis of incomplete abortion. A curettage was performed, the convalescence was smooth and the patient was discharged at the end of 12 days, apparently well. She was readmitted, however, 12 days later with an obvious general peritonitis and was desperately ill for five days, after which she showed satisfactory improvement for six days. During this time, she had received three blood transfusions, adequate doses of sulfanilamide, continuous gastric drainage and copious amounts of fluids by vein. On the fourteenth day of her second admission, her temperature rose to 103° F and she complained bitterly of pain in the left shoulder and neck, the pain being increased on deep inspiration. There was tenderness over the left trapezius muscle. A left subphrenic abscess was suspected, and this diagnosis was substantiated by finding a high, fixed diaphragm on the left side on fluoroscopic examination, and by demonstrating downward and medial displacement of the barium-filled stomach. A two-

stage transpleural approach was made at the level of the ninth rib in the midaxillary line, and a subphrenic abscess containing 300 cc of thick *Staphylococcus pus* was evacuated. Her subsequent course was satisfactory, and she was discharged as well, 40 days after operation.

COMMENT—In this instance, the correct diagnosis of left subphrenic abscess was promptly and accurately made. This was largely due to the interest now being taken in this Clinic in this condition. The roentgenogram, taken in the Trendelenburg position, after the ingestion of a barium meal demonstrated the condition very well.

Treatment—The proper treatment of a left subphrenic abscess is adequate drainage as soon as feasible after the diagnosis is made. An abscess lying in the anterior intraperitoneal space is best drained extraperitoneally, through an incision just below the costal margin if it presents anteriorly. If it cannot be palpated below the costal margin, a transpleural approach at the level of the eighth or ninth rib in the midaxillary line should be employed. Abscesses in the lesser peritoneal cavity should be drained through a celiotomy, and by an opening in the transverse mesocolon or gastrohepatic omentum, depending upon where the abscess is presenting. Extraperitoneal abscesses may be drained by an incision in the lumbar region directly over them.

One of the six patients in this series refused operation, two of the six patients had their abscesses drained through a transpleural approach, one through the transperitoneal route and in two others the subphrenic abscess, which had ruptured through the diaphragm, was drained at the time of the thoracotomy for the empyema.

CONCLUSIONS

(1) The occurrence of subphrenic abscess on the left side has not been emphasized enough heretofore, most of the attention has been directed to the right-sided abscess. Statistics indicate that, of every four or five subphrenic abscesses, one will be on the left side.

(2) Subphrenic abscess on the left is more difficult to diagnose by physical examination than is the right-sided variety.

(3) The roentgenologic and fluoroscopic diagnosis of left subphrenic abscess can be simplified and made more certain by examining the patient after the stomach has been filled with barium.

(4) Six cases of left subphrenic abscess are reported in detail. They emphasize the fact that these abscesses are diagnosed late, and often only then, because of rupture into the pleura, into a hollow viscus or into the peritoneal cavity.

(5) Suppuration in the pelvis, especially postpartum infection, is frequently the cause of left subphrenic abscess.

REFERENCES

- ¹ Ochsner, Alton, and Graves, A. M. Subphrenic Abscess—Analysis of 3,372 Collected and Personal Cases. *ANNALS OF SURGERY*, 98, 961, 1933.
- ² Barnard, H. L. Surgical Aspects of Subphrenic Abscess. *Brit Med Jour*, 1, 371-429, 1908.

LEFT SUBPHRENIC ABSCESS

- ³ Lockwood, A L Subdiaphragmatic Abscess Surg, Gynec and Obstet, 33, 502, 1921
- ⁴ Schwartz, J Suppuration in the Subphrenic Region Arch Surg, 20, 317, 1930
- ⁵ Beye, H L Thoracic Complications of Subdiaphragmatic Abscess Jour Thoracic Surg, 1, 655, 1932
- ⁶ Gatewood Subphrenic Abscess Am J Med Sci, 180, 398, 1930
- ⁷ Elkin, D C Subphrenic Abscess J A M A, 97, 1279, 1931
- ⁸ Fifield, L R, and Love, R S M Subphrenic Abscess Brit Jour Surg, 13, 683, 1926
- ⁹ Gogol, L J Subphrenic Abscess Surgery, 3, 386, 1928
- ¹⁰ Overholt, R H, and Douchess, J E Subphrenic Abscess New England Med Jour, 213, 294, 1935
- ¹¹ Ochsner, Alton Subphrenic Abscess New Orleans Med and Surg Jour, 81, 102, 1928
- ¹² Ochsner, Alton, and Nother, Carl Retroperitoneal Operation for Subphrenic Abscess Surg, Gynec and Obstet, 37, 665, 1923
- ¹³ LeWald, L T Subphrenic Abscess and its Differential Diagnosis Roentgenologically Considered Arch of Surg, 10, 544, 1925
- ¹⁴ Lehman, E P The Place of Exploratory Operation in the Surgery of Subphrenic Abscess ANNALS OF SURGERY, 106, 514, 1937
- ¹⁵ Steele, J D Subphrenic Abscess with Bronchial Fistula ANNALS OF SURGERY, 105, 496, 1937
- ¹⁶ McNamee, E P Subphrenic Abscess Am J Roent and Rad Therap, 24, 125, 1930
- ¹⁷ Granger, A Radiological Signs of Subdiaphragmatic Abscess New Orleans Med and Surg Jour, 82, 748, 1930
- ¹⁸ Delario, A J Subdiaphragmatic Abscess Am J Roent and Rad Therap, 31, 177, 1934
- ¹⁹ Pancoast, H K Roentgenological Diagnosis of Liver Abscess with or without Subdiaphragmatic Abscess Am J Roent and Rad Therap, 16, 303, 1926
- ²⁰ Santa, L R Pneumoperitoneum as an Aid in the Diagnosis of Subdiaphragmatic Conditions J A M A, 80, 464, February 17, 1923

DISCUSSION —DR ALTON OCHSNER (New Orleans, La) The Association is indebted to Doctor Carter for calling attention to the relatively frequent occurrence of left-sided subphrenic abscess I should like to show briefly our modification of Bernard's localization of the subphrenic abscess

Surgically the subphrenic space is bounded above by the diaphragm and below by the transverse colon and mesocolon There are three spaces on the right and three on the left Those on the left, we have divided into two below the liver, the antero-inferior space and a postero-inferior space, which is the lesser peritoneal sac There is a single space above the liver That is due to the fact that the left prolongation of the suspensory ligament runs in an oblique angle, extending posteriorly on the left

About a year ago Doctor DeBakey and I collected 1,531 cases of subphrenic abscesses, and found that 906 of them, or 59 per cent, were on the right side This included our own cases Fourteen per cent were retroperitoneal, and 27 per cent, or approximately a fourth, were left-sided Sixty-eight, or almost 5 per cent, were combined

To break this down, one finds that of the left-sided abscesses, the left antero-inferior, which is the space which Doctor Carter referred to, is most frequently involved The left superior, that is, above the liver and between it and the diaphragm, was involved next most frequently, or approximately 4 per cent, and the lesser side in a smaller percentage

Doctor Carter's diagnostic test is certainly a desirable one because it is

difficult to make a diagnosis of left-sided subphrenic abscesses. Probably the greatest difficulty is not thinking of the possibility.

I do not believe that any patient with a subphrenic abscess should be allowed to develop a pleural effusion. They develop it only because of the delay in the diagnosis.

I want to emphasize the importance of draining subphrenic abscesses extracapsularly when it can be done. The mortality rate in our series of 36 cases of subphrenic abscess drained extracapsularly is 6 per cent as contrasted with the mortality rate of most of the reported cases varying from 25 to 75 per cent.

DR STUART HARRINGTON (Rochester, Minn.) I was very much interested in Doctor Carter's presentation of the subject of left subphrenic diaphragmatic abscess. He has emphasized the difficulties associated with their recognition which often led to a late diagnosis. I was particularly interested in his comment upon the fact that these abscesses occasionally rupture through the diaphragm into the lung and empty into the bronchus. I should like to call attention to a late surgical condition which occasionally results from a rupture of a left subdiaphragmatic abscess through the diaphragm into the lung. The abscess produces inflammatory necrosis of the diaphragm and often produces a large opening through the diaphragmatic muscle at the point where it ruptures into the lung. If the drainage of the abscess is complete, the abscess may heal and later the stomach may herniate through this opening in the diaphragm. This, however, is not a common cause of diaphragmatic hernia, it was the etiologic factor in only three of the 210 cases of diaphragmatic hernia upon which I have operated. The following case is an instance of this type upon which I operated in 1931.

Case Report—The patient was a law student, age 22 who had been taken suddenly ill at night following a banquet, ten months before his admission. He had had severe epigastric pain which had become more or less generalized and his temperature had reached 104° F. Later, pain had developed in the left subphrenic region and vomiting had occurred. Immediate operation had been considered but was not performed because of the diffuse character of the symptoms. The course of the disease remained septic for three weeks. The pain and tenderness then had become localized in the left upper quadrant of the abdomen. Four weeks after the onset, the patient had had a severe attack of coughing during the night, and had coughed up about one quart of pus. A general decrease in the cough and expectoration had occurred during the next two months, with cessation of thoracic and abdominal symptoms. The patient had gained 25 pounds. His condition had gradually improved and all of the abdominal symptoms had disappeared.

He had returned to his work and after about one month pain had developed in the left side of the upper part of the abdomen on taking food. This pain had been referred to the left shoulder, it had not been related to any particular type of food. His breakfast and midday meals had been rather light and he had had little discomfort after these meals. The evening meal had been heavy, and following this he had had most of his trouble. Three months after the onset of these symptoms he had begun to vomit when the stomach was full. This had become progressively more severe and of retention type. He often had vomited large quantities, two quarts at a time, and the vomitus often had contained coffee-ground material. All of his symptoms had been relieved as soon as the stomach had been emptied, or by vomiting.

The roentgenograms of the stomach and esophagus showed elevation and fixation left side of diaphragm, the stomach was fixed to the diaphragm. On reexamination, the same diagnosis was made. Because of his symptoms, which were very suggestive of hernia, operation was advised. Operation disclosed that practically the entire stomach had herniated through a large opening in the left leaf of the diaphragm. There was also

herniation of three or four feet of the transverse colon. An enormous number of adhesions were present throughout the entire left half of the upper part of the abdomen and the herniated viscera were very adherent to the margins of the opening, which was situated about 2 cm. to the left of the esophageal opening, in the posterior portion of the left half of the diaphragm. The herniated viscera were replaced in the abdomen and the abnormal opening in the diaphragm was closed with interrupted silk sutures and continuous sutures of fascia lata. His convalescence was uneventful and he made a satisfactory recovery.

This case is of particular interest not only because of the infrequency of the occurrence of left subphrenic abscess but also because of the rare occurrence of complete healing of left subphrenic abscess following traumatic rupture through the diaphragm and into the lung. It is also of particular interest because of the occurrence of diaphragmatic hernia through the site of rupture of the abscess through the diaphragm. The clinical evidence was the most important factor in establishing a diagnosis in this case. The roentgenogram before operation did not disclose the presence of a hernia but revealed that the stomach was adherent to the undersurface of the diaphragm and was causing obstruction. This was due to the fixation of the lung around the margins of the diaphragm on the pleural side. The lower margin of the lung gave the appearance of the diaphragm but at the time of operation it was found that the stomach had herniated through the opening and was fixed to the undersurface of the lung rather than to the diaphragm. While this is an infrequent cause of diaphragmatic hernia, I have seen two subsequent incidences, and in these cases the interval between the onset of the acute abdominal condition and the symptoms of the hernia were much greater. In one case, several years had elapsed before the diagnosis of diaphragmatic hernia was established.

DR EVARTS A. GRAHAM (St. Louis). I wish to add an additional feature to this presentation and also to the discussion of Doctor Ochsner, and that is that occasionally a subphrenic abscess is not limited to a single space such as has been portrayed by the speaker. I am not referring to bilateral subphrenic abscess, but a subphrenic abscess on one side of the body which is not necessarily confined to a single space. For example, not long ago I had a patient with a subphrenic abscess in what Doctor Ochsner would call the left antero-inferior space, from which space I obtained about 500 cc. of pus. He improved somewhat, but did not recover, and it was necessary to operate upon his left postero-inferior space, at which time about 300 cc. of additional pus was obtained, after which the patient made an uneventful recovery.

I have seen at least one other patient, similar to the case cited above, in whom pus was multilocular, that is, occupying more than one space, when it occurred on the left side.

DR ROSCOE R. GRAHAM (Toronto, Canada). May I express my appreciation for the information so ably presented on this interesting and difficult subject. We have observed, following abdominal operation, upon patients under spinal anesthesia, that postoperative roentgenograms of the abdomen will show that gas is present under the diaphragm for as long as three weeks following operation. The importance of appreciating this fact becomes obvious in a patient who is doing badly following operation, and in whom one might suspect a subphrenic abscess as the cause. Thus, it would be obvious that the presence of a gas bubble under the diaphragm within three weeks post-operative, if the patient had been operated upon under spinal anesthesia, would not be evidence of subdiaphragmatic suppuration. (Lewis, F. I. J. A. M. A., 28, 18, 1938.)

EXTRAPLEURAL PNEUMOTHORAX*

HORACE BINNEY, M D

BOSTON, MASS

THE OPERATION of extrapleural pneumothorax has brought a new method to our aid in the treatment of tuberculous cavities in the lung. Although suggested by Tuffier as far back as 1891, and demonstrated as practical in single or small groups of cases by continental surgeons during the past few years, the method did not meet with general acceptance until the reports, in 1937, by Graf³ and Schmidt,¹ of 107 and 155 cases, respectively. Their low operative mortality and the rapid symptomatic improvement, as well as conversion of the sputum, plus the comparative simplicity of the procedure in suitable cases, brought it into immediate favor.

Recent reports by surgeons of several countries agree as to low mortality and beneficial effect of rapid closure of cavities by selective collapse of the diseased area, but all agree in the necessity of prolonged maintenance of the air-pocket. Therefore, the operation being of so recent origin, not enough time has elapsed for any reports of final results, but, for the reasons already mentioned, and especially the lesser gravity of the operation as compared with thoracoplasty, the general opinion has been, to use the words of Coryllos,² "that it is well worth trying."

Also, in recent reports there has been shown a close similarity as to technic with that described by Graf and Schmidt. The adherence to strict indications, however, has evidently not been as close, and the result has been the application to cases which were apparently not suited to the method. It seems, therefore, important for the guidance of those beginning the use of this operation, to report unfavorable results as well as successes, which is the purpose of the present communication.

For the sake of clearness, it may be well to briefly review the indications for this operation and the technic as laid down by the principal writers who have already reported their experiences.

As the name implies, the aim of the operation is to produce a selective collapse of the part of the lung involved, usually the apex, by means of an air-pocket made by stripping the pleural layers off the inner surface of ribs and intercostal muscle sheaths. The production of this extrapleural space causes a collapse of the lung, varying in amount with the extent of the stripping, the maintenance of which depends on two factors: (1) Tight closure of the innermost layer of chest wall tissue to form a complete air sac for compression of the lung, and (2) repeated injections of air into this space for a prolonged period in order to obtain healing of the obliterated cavity. The latter part of the treat-

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

ment is quite the same as in intrapleural pneumothorax with certain minor differences

Indications—The indications for the operation as given in more recent articles are as follows

- (1) Cases with apical cavernous disease with complete pleural symphysis, or apical adhesions too extensive to be dealt with by intrapleural pneumolysis
- (2) More extensive unilateral disease with pleural symphysis, but whose vital capacity is great enough to tolerate a sudden and extensive collapse. From our own experience we place the minimum at 1,500 cc in such cases
- (3) Cases where, owing to concurrent cardiac disease, old age, asthmatic or emphysematous condition, thoracoplasty is contraindicated
- (4) Growing children where thoracoplasty is undesirable
- (5) Early stages of the disease. Certain writers (Sellors⁴ and Overholt⁵) have included, as an indication, a stage, presumably with cavity already formed, which is too early to allow thoracoplasty owing to poor condition, toxemia, etc., and lowered resistance. From an experience (Case 2) in which the operation, although performed under local anesthesia, was followed by a rapid spread in both lungs and death in eight weeks, we believe that extrapleural pneumothorax must be regarded as having a very definite risk in these cases. The rapid and extensive collapse which may follow doubtless breaks down local barriers to the spread of the disease, which may overcome resistance, local and general. We believe the inclusion of early cases, or of doubtful resisting powers, should be exceptional

To the above list, possibly those cases should be added where repeated hemorrhages threaten to seriously reduce the patient but have not yet made operation too hazardous. While we have not treated any hemorrhage cases with extrapleural pneumothorax, it would seem to be indicated in certain cases.

Contraindications—Since the possibility of successful production of the extrapleural air-pocket depends upon the absence of too firm adhesions between parietal pleura and chest wall, a very chronic condition with extensive or very dense lesions, especially with large cavities near the periphery, is a contraindication. There are three reasons for this

- (1) There may be no line of cleavage in the endothoracic fascia, so that separation is practically impossible
- (2) The danger of rupture of a thin-walled cavity, either during operation or later, is too great
- (3) In thick-walled cavities it may be impossible to produce collapse even with positive pressure

In these conditions, thoracoplasty is likely to be safer and more efficient

Large cavities, unless centrally located and of not too great chronicity, are

also a contraindication, owing to danger of rupture. The occurrence of pulmonary fistula has been mentioned often enough in the published reports to prove that rupture of the cavity wall after operation is not rare (Overholt,⁵ Sellois,⁴ Pierre-Bougeois and Lebel⁶). In the stripping-off of the fused pleural layers, the blood supply of a superficial cavity wall may well be destroyed. In long-standing disease, especially, it is probable that the chief blood supply of at least the peripheral aspect of the cavity is from small branches of the intercostal vessels which of course are ruptured in the stripping process. Therefore, we believe that a superficial cavity of more than 2.5 cm. is a contraindication, and that in such a case a thoracoplasty is far safer.

Activity—As suggested in the discussion of *Indications*, active or too early lesions are a definite contraindication for reasons already stated.

Technique—In the posterior approach, which we have used exclusively, the exposure of the extrapleural layer is made by an incision through the trapezius and rhomboid muscles, long enough to afford access to the fourth rib and allow subperiosteal removal of about four inches. The length and direction, whether vertical or oblique, will depend upon thickness of the muscles and, according to the surgeon's choice, whether the muscles are cut transversely or split between muscle bundles.

Coryllos² preferred resection of the third rib and the end of the corresponding transverse process, which exposes the third intercostal nerve lying on the endothoracic fascia and serves as a guide to the line of cleavage. Sellors⁴ advises an oblique incision, division of two ribs near the spine without removal, spreading of the ribs after freeing the periosteum. He states that closure with a periosteal suture is easy to obtain.

We have employed an incision 2 to 3 cm. within the vertebral border of the scapula in the majority of our series.

The incision of the periosteal bed of intercostal muscle (Roberts⁷) must be made with great care in order not to injure the parietal pleura. The endothoracic fascia in most cases is a rather loose areolar layer of tissue, and the stripping is done *in this layer*, rather than between it and the parietal pleura (Coryllos), and the presence of fat is sometimes a guide to this layer (Overholt). Roberts advises incising the intercostal muscle rather than the periosteum to protect the underlying pleura from injury, but we believe this makes the final tight closure more difficult. The stripping is best begun by a wiping of the pleura with a gauze pledget held in a suitable clamp, but when once started the stripping of loose adhesions can be done with the finger, especially as the axillary region is approached. The apex should be freed as thoroughly as possible on all sides, and the stripping carried all around the diseased lung and to a level below the lesions in order to provide a "reserve of compression" (Schmidt). Overholt advises stripping to two rib spaces below the roentgenologic level of the cavity. This allows for possible readhesion at the lower margin of the air-pocket between refills. In order to control hemorrhage from torn vessels, an electric illumination of the cavity is indispensable, to render bleeding points visible. While smaller ones will close with brief pressure with

a gauze pack, larger ones may require clamping, or even inclusion in a silver clip or ligature

Postoperative hemorrhage has been a serious complication in some reported cases and must be prevented by careful hemostasis before closure is begun. Overholt has devised flat ribbon retractors bearing an electric light at the end to facilitate this important step

Extensive pleuritis may have produced dense bands which require cutting but this is unusual in our experience. Of course, occasionally an extreme degree of extrapleural fibrosis ("pachyexopleurite" Pierre, Bougeois and Lebel) may render the stripping too difficult and the operation must be abandoned in favor of thoracoplasty

The final closure of the periosteomuscular layer is accomplished by a continuous suture of fine catgut, which can be made easier by division of the periosteum of an adjacent rib and separating it sufficiently from the rib to relax the tissues at the suture line. Any possible gaps, through which air leakage may occur, should be reinforced by a muscle flap, for which the serratus superior often serves

Before the patient is removed from the operating table, an injection of 50 to 100 cc of air should be made, raising the manometer pressure reading to about $+5$ cm

After-Treatment—Frequent refills should be carried out, especially during the first few days. As the air absorption may be rapid at first, refills every 12 hours for the first day or two may be necessary, the interval being gradually lengthened to every two days at the end of the week, and to once a week by the end of the month. If air is lost through emphysema, lower pressures and more frequent refills are necessary, but as healing of suture line and tissue spaces occurs, higher pressures are employed to maintain the collapse. Fluid, somewhat bloody at first, should be aspirated. Roentgenologic control of the air-pocket is of the greatest value. If this shows the floor of the pocket to be rising through readhesion at the margins, injection of sterile oil, as used by Schmidt, Brunner,⁸ and others, should be resorted to. We have found this very useful. After the air-pocket becomes tightly sealed, pressures may be raised to $+15$ or $+20$ cm

Higher pressures carry the danger of rupturing the cavity wall, which occurred in one of our cases. Escape of air through the suture line, forming an air-pocket under the muscles of the back, is another possibility

Duration of Treatment—As the situation after the establishment of an extrapleural pneumothorax (or oleothorax) is similar to an intrapleural pneumothorax, which requires two years or more for successful healing of the cavity, the treatment should be carried out at least as long. The operation is, therefore, too recent for any report on final results to be available

Complications—Postoperative hemorrhage into the air-pocket, perforation of the cavity wall, fistula, and resulting extrapleural empyema are the principal complications, any one of which may cause a fatality, or failure to maintain

collapse, which will demand a subsequent thoracoplasty. This occurred seven times in Schmidt's series of 155 cases.

Results—The largest series of cases as yet reported is that of Schmidt. In 155 cases, there were two operative deaths following extrapleural pneumothorax, an operative mortality of 1.2 per cent. There were nine deaths later, a total mortality of 7 per cent, 52 cases required oleothorax, 124 showed a satisfactory collapse.

Experiences and Results with 32 Cases at the Boston Sanatorium—During the past 14 months, extrapleural pneumothorax has been attempted or carried out in 33 cases, in one of which firm adhesions prevented stripping of the pleurae from the chest wall, and thoracoplasty was performed. Of the 32 cases in which the extrapleural operation was performed, all were cases of more or less advanced disease of a duration varying from ten months to 16 years. Thirty cases were of unilateral, and two of bilateral, apical disease. All were performed under local anesthesia (novocain) preceded by morphine and scopolamine, and supplemented by gas-oxygen inhalation, during the process of stripping the pleura, in most cases. In only one case was there a severe degree of shock, in all others this was slight or moderate. Two cases died, one (J. D., Case 1) on the twelfth day, the second (J. R., Case 2), after two months, the latter having bilateral disease.

In the first two cases operated upon, the stripping was not carried far enough and the resulting air-pocket was insufficient to produce effective collapse and, while the cough and expectoration were greatly diminished, the sputum remained positive. One of these has had a secondary operation after ten months of refills. This operation was carried out without difficulty and a large air-pocket established. In the other case, the patient has so far refused a second operation.

In the third case to be operated upon a small air-pocket was quickly lost through air leakage and adhesions reforming, and a thoracoplasty was performed four months later. Although a second stage has been recently carried out, the sputum is still positive.

Seven cases have been discharged from the hospital in good physical condition and with negative sputa, and are returning every week or two for refills.

In several of the earlier cases, air was injected under excessive pressure, which in two cases resulted in escape of air under the back muscles rendering the collapse less effective, and in a third case a pulmonary fistula developed, causing infection of the air-pocket, which is now being kept open by a drain and irrigated. The sputum remains positive. The final result is uncertain as the collapse is insufficient (Fig. 1 and 2).

Collections of fluid, at first bloody, later becoming serous occurred in 15 cases (47 per cent) and of these eight were treated by aspiration when refills were undertaken. In two, the fluid became purulent and gomenol has been injected, apparently with good effect. One purulent case has developed a spread to the other lung.

EXTRAPLEURAL PNEUMOTHORAX

(Before)

(After)



FIG 1

FIG 2

Figs 1 and 2—Medium sized cavity left upper lobe. Disease of three years' duration. Small air pocket obtained. High pressures used probably excessive as fistula developed through cavity wall. Drainage sinus developed in operation wound. Picture shows lipiodol in bottom of air pocket, below level of fistula.

(Monaco)

(Johnson)

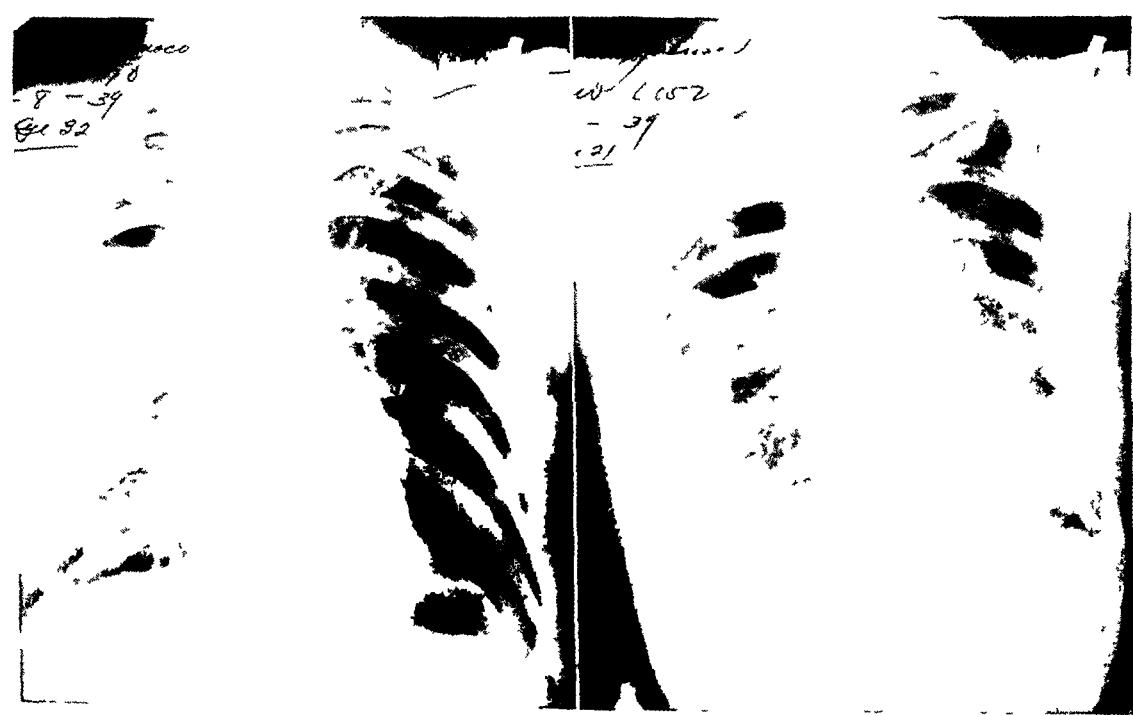


FIG 3

FIG 4

FIG 3—Illustrating case in which good collapse obtained with large air pocket, and sterile effusion (serous).
FIG 4—Illustrating bilateral disease, operated upon in two stages. Complete relief of symptoms and conversion of sputum.

In 27 cases of the 32, a satisfactory air-pocket was obtained, and in 20 (62 per cent) a conversion of sputum effected

Summary of results

Operation impossible, requiring thoracoplasty	1 case
Extrapleural pneumothorax carried out	32 cases
Fluid (sterile) developed	15 cases (47 0%)
Fluid (purulent) developed	2 cases (6 2%)
Satisfactory collapse obtained	27 cases (84 3%)
Collapse unsatisfactory, requiring later operation (thoracoplasty)	3 cases (9 2%)
Conversion of sputum	20 cases (62 0%)
Cases made outpatients	7 cases (21 8%)
Deaths	2 cases (6 2%)

ANALYSIS OF FATALITIES

Case 1—J D, female, age 32, single, was admitted, April 12, 1938, with a history of phthisis of 11 years' duration. Treated at other sanatoria from 1927 to 1931, during which time a right phrenicectomy was performed, then at home until admission. Examination

(D Amato)



FIG 5—Case 1. Large cavity in right upper lobe. At operation, good collapse obtained and 150 cc air injected into extrapleural pocket. After third day, increasing dyspnea due to rupture of cavity wall, partially relieved by daily removal of air. Death on twelfth day.

showed normal temperature, respirations 20 to 24, slight cyanosis, signs of involvement of right apex, right diaphragm high. Sputum positive, two ounces in 24 hours. Attempts at pneumothorax unsuccessful. During next six months, large cavity developed in right upper lobe. Left lung showed few rales at apex but negative roentgenologically. General condition fair. Vital capacity = 1,000 cc (Fig 5).

Owing to failure to improve, and increase in size of cavity, extrapleural pneumothorax

EXTRAPLEURAL PNEUMOTHORAX

decided upon, and performed under local anesthesia, October 28, 1938. During operation, patient showed marked shock, but with stimulation and intravenous glucose, operation completed, and 150 cc of air injected into air-pocket. Patient placed in oxygen tent. Condition improved during next three days under continuous oxygen. On fourth day, increased dyspnea present. Pressure in air-pocket found positive and 75 cc air removed. Relief only temporary. Fluid and air removed daily but pressure continued positive, evidently due to a rupture of the cavity wall. Patient gradually failed, and died on 13th day, with signs of bronchopneumonia in left lung. No autopsy.

In this case, the low vital capacity and large cavity near the periphery of the lung should have warned us against even extrapleural pneumothorax.

Case 2—J. B., male, Negro, age 22, married, was admitted, March 29, 1938, with history of three months' cough and loss of weight. Sputum found positive one week pre-

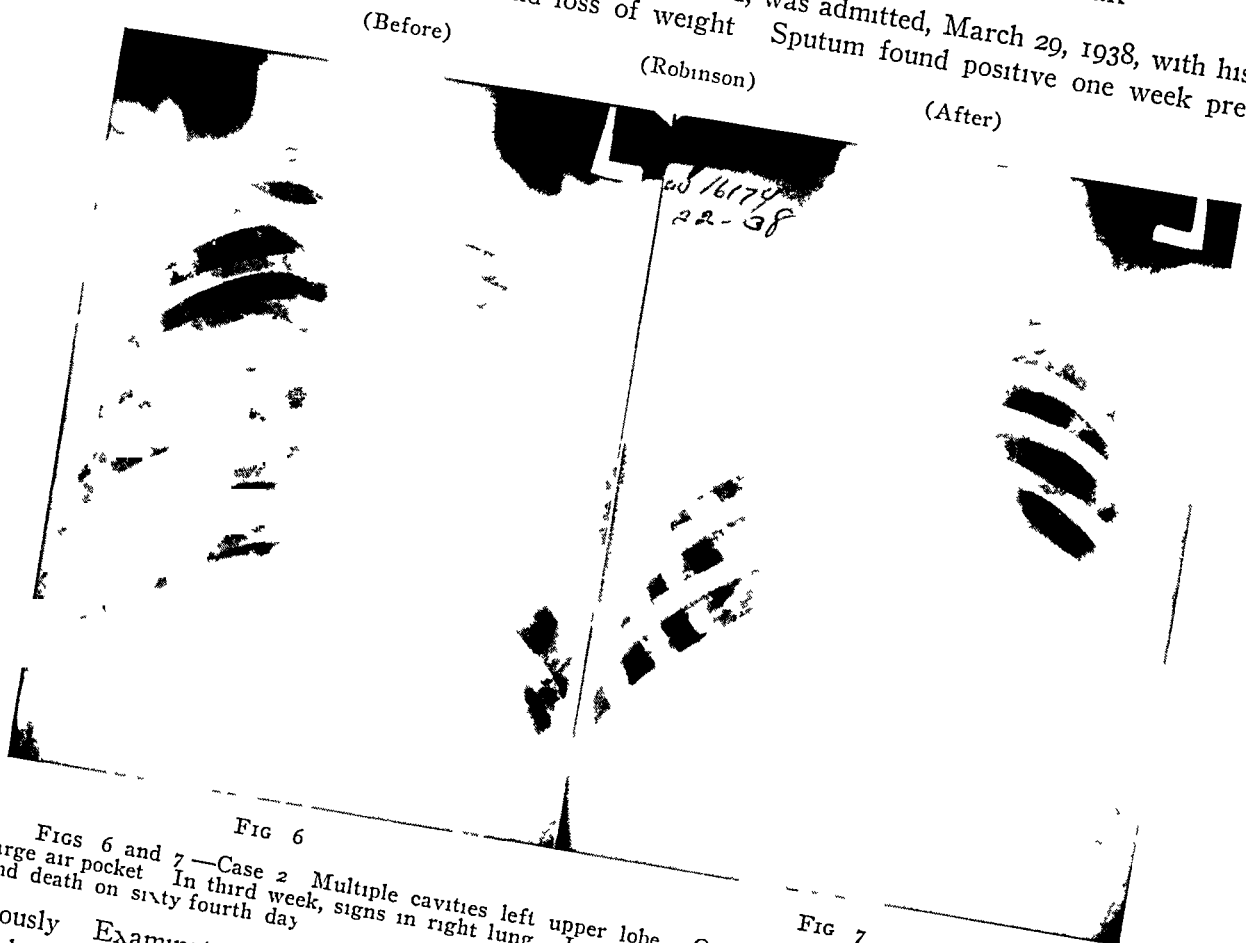


FIG 6

FIG 7

Figs 6 and 7—Case 2. Multiple cavities left upper lobe. Increase of cough and sputum, finally hemorrhage and death on sixty fourth day.

Examination showed a pale, poorly nourished patient with diffuse involvement of both lungs, especially marked in left upper lobe. Put on bed rest for three months. After several unsuccessful attempts at pneumothorax, a left phrenic paralysis performed. During next three months, ran a moderate temperature. Condition in right lung improved, left remaining unchanged. Roentgenograms showed density of left upper lobe, clinical signs of cavity present. Extrapleural pneumothorax advised, and performed, October 21, 1938. Good collapse obtained but cough soon increased, temperature more elevated, and signs of spread to right lung appeared. After a month, a severe hemorrhage occurred and right intrapleural pneumothorax given without success in control of streaking. Patient failed and died four days later, 64 days after operation. Autopsy showed extensive fibrocavernous disease in both lungs, more marked on the left side (Figs 6 and 7).

This patient evidently had not developed sufficient resistance to stand the rapid and extensive collapse of the more diseased lung. The prognosis in a

Negligence being poor under any conditions, the attempt to prevent further extension of the disease by surgery was an error in judgment

CONCLUSIONS

Extrapleural pneumothorax has the advantage of being suitable for local anesthesia, of having less shock, and a lower rate of mortality than thoracoplasty. It cannot, however, be safely applied in early cases with low resistance, nor is it suitable in large cavities or in those over 2.5 cm. in diameter, when very superficial, nor in long-standing cases with dense lesions. Here the pleurae are likely to be too adherent to the chest wall, and thoracoplasty is necessary. While rapid in symptomatic benefit, and often in conversion of sputum, the after-treatment with refills must be prolonged—how long we are not yet in a position to judge.

REFERENCES

- ¹ Schmidt. *Revue de Tuberculose, Paris*, 3, 1122, 1937
- ² Coryllos. *Bulletin of Sea View Hospital*, 3, 264, 1938
- ³ Graf. *Deutsche med. Wochenschr.*, 62, 674, 1936
- ⁴ Sellors. *Brit. Jour. Tuberculosis*, 32, 182, 1938
- ⁵ Overholt. *Jour. Thor. Surg.*, 7, 591, 1937-1938
- ⁶ Pierre-Bourgeois and Lebel. *Monde Medical*, 920, 665, 1938
- ⁷ Roberts. *Brit. Jour. Tuberculosis*, 32, 68, 1938
- ⁸ Brunner. *Schweiz. med. Wochenschr.*, 68, 729, 1938

ADDITIONAL REFERENCES

- Brock. *Brit. Jour. Tuberculosis*, 32, 193, 1938
Belsey. *Jour. Thor. Surg.*, 7, 575, 1938
Maurer and Savitsch. *Lancet*, 2, 1468, 1938

BOWEL OBSTRUCTION IN THE NEW BORN⁺

EDWIN M. MILLER, M.D.

CHICAGO, ILL.

FROM THE SURGICAL SERVICE OF THE PRESBYTERIAN AND COOK COUNTY HOSPITALS, CHICAGO, ILL.

THE INFANT presenting evidence of bowel obstruction immediately after birth or within the first few days of life deserves the best attention of the pediatrician and the surgeon. Fortunately, these cases do not occur often, but perhaps this relative infrequency of occurrence itself may cause the physician who first sees the baby to overlook the likelihood of a real obstruction, and, therefore, to delay surgical interference too long. I feel sure that this may be accountable for some unnecessary deaths.

The frequency of occurrence of a congenital obstruction in the new born, excepting of course the not uncommon imperforate anus, is difficult to estimate accurately. No report of this kind appeared in the literature until that of Calder¹ of Edinburgh, in 1733. Thieremin,² in 1877, found only nine cases in 150,000 autopsies in the Foundling's Hospital in St. Petersburg. Tandler³ of Vienna, in 1900, collected 94 reports, and Davis and Poynter⁴ of Omaha, in 1922, had gathered a total of 392. Up to the present time, well over 500 cases have been recorded, and most authors seem to feel that perhaps 1 in 20,000 infants at birth are thus affected.

Many different theories have been advanced to explain the wide variety of pathologic conditions that may produce a partial or complete congenital obstruction, yet the probabilities are that the great majority of them can easily be interpreted on the basis of errors or defects in embryologic development. The very fact that most of them are located in the duodenum near the ampulla of Vater, and the terminal ileum close to Meckel's diverticulum, strongly supports the contention that these anomalies occur at the sites of the most complex embryologic changes, an opinion first stated by Bland-Sutton⁵ in 1889.

The pathology is well understood. The literature concerned with congenital bowel obstruction up to within the last 25 years was almost a continuous, uninterrupted series of autopsy reports and citations of fatal cases, as it was not until 1911 that the first successful operation for atresia of the ileum was performed by Fockens⁶ of Rotterdam, and not until 1916 that Einst⁷ of Copenhagen published the first successful operation for atresia of the duodenum. These two papers still stand as milestones in the field of intestinal surgery in infants. In general, two main types of pathology are recognized: (1) The intrinsic, consisting usually of a complete gap or interruption in the continuity of the bowel, sometimes a cord-like remnant of the lumen insufficient in caliber to permit the passage of intestinal content, and, more rarely,

⁺ Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

a septum or mis-like diaphragm acting as a partition to block the channel (Seidlin,⁸ and Garvin⁹) (2) The extrinsic, caused by abnormal folds of peritoneum, adhesions left by fetal peritonitis, direct pressure from overlying large vessels (*i.e.*, the root of the mesentery across the third portion of the duodenum), or a faulty rotation of the cecum or ascending colon, leading to a volvulus of the midgut on the axis of the superior mesenteric artery and abnormal fixation of the cecum in a position where it partially or completely blocks the duodenum close to its junction with the jejunum Davis and Poynter,⁴ in their analysis of 392 recorded cases up to 1922, showed that 134 occurred in the duodenum (59 above the ampulla, and 75 below it), 60 were in the jejunum, 101 were found near or at the terminal ileum, and only 39 in the colon In 76 instances the lesions were multiple

Early recognition of an obstruction in the new born is essential if successful results are to be expected and the high mortality materially reduced The physician first to see the infant must, therefore, be alert to the possibility of its presence In the differential diagnosis of every case of pylorospasm or congenital pyloric stenosis, especially in the absence of a palpable tumor, and particularly if the vomiting begins early (after the first nursing or within the first few days of life), one must always consider the possibility of a partial or complete obstruction in the first portion of the duodenum The presence of bile in the vomitus gives one a valuable clue, and the clinical picture of persistent biliary vomiting coupled with visible peristaltic waves in the epigastrium, a flat lower abdomen, and rapid dehydration is almost unmistakable evidence of an obstruction of the duodenum below the ampulla of Vater, in all probability due to a true atresia, pressure from the overlying superior mesenteric vessels, or a twist at the duodenojejunal junction A persistent vomiting which soon becomes fetid in odor and brown in color, and is associated with general abdominal distention and obstipation can mean only one thing, *i.e.*, a partial or complete obstruction lower down, probably in the terminal ileum In any case where a doubt exists, it is a wise plan to verify one's suspicion roentgenologically, by giving a little thin barium mixture by mouth if the obstruction seems to be high, or by giving barium as an enema if the obstruction seems to be low In the former, the exact lower limit of the obstruction can thus be easily demonstrated, and in the latter, the visualization of the collapsed colon will help to confirm one's impression of the lesion being proximate to the ileocecal valve

What chance, you may ask, has a new born baby thus afflicted, with a complete or almost complete obstruction in the duodenum or small bowel, to survive beyond a period of a few days or at most a few weeks? I can best answer that question by referring to the evidence from the literature and adding to that evidence certain impressions which I have gained from my own experience

Group A If the obstruction is in the *jejunum* or *ileum*, the chances of recovery are very small, because, during a period of over 100 years, there have been only three successful results reported

Case 1—Fockens, P,⁶ Rotterdam, 1911 Vomiting since birth becoming fecal in character On seventh day after birth brought to hospital Abdomen distended and tympanic Visible peristalsis At operation on eighth day, a gap in lower ileum 4 cm long bridged by fibrous cord *Lateral anastomosis* Recovery

Case 2—Demmer, Fritz,¹⁰ Vienna, 1921 On September 22, 1921, new born infant brought to hospital, presenting evidence of a tumor in region of navel and complete obstruction of small bowel At operation an atresia of terminal ileum with 14 cm gap Resection of vestige of cecum *Lateral anastomosis* Recovery

Case 3—Carter, R F,¹¹ New York, 1933 Infant four days old No bowel movement since birth Fecal vomiting for 12 hours Moderate distention and visible peristalsis At operation an atresia of lower ileum with cord-like structure attaching it to the cecum Proximal bowel greatly dilated, distal collapsed *Lateral anastomosis* between ileum and descending colon *Ileostomy* proximal to anastomosis Recovery

COMMENT—Anyone who has had experience with this type of case will be able to appreciate the reasons for the high mortality in this group The baby is usually in poor condition when it comes to operation, the proximal bowel is not only greatly dilated but often beginning to show signs of necrosis The distal bowel has never functioned and is collapsed—usually the size of a small lead pencil Even if a lateral anastomosis can be made, the thick, viscid meconium in the distended bowel cannot readily pass on into the distal segment There has never been a successful result recorded where ileostomy alone has been used

Group B If the obstruction is in the *duodenum* and produces a complete or almost complete block of the lumen, which requires some sort of short circuiting anastomosis, the outlook, while still bad, is considerably brighter than in Group A Moreover, the prospects for still better results are very encouraging In this group successful operative results are limited to the following 16 cases

Case 1—Ernest, N P,⁷ Copenhagen, 1916 Male infant Vomiting began with first feeding and continued Rapid loss of weight Dehydration Operation on eleventh day showed duodenum greatly dilated down to upper margin of transverse colon Jejunum collapsed *Duodenojejunostomy* (antecolic) Recovery

Case 2—Weeks, A, and Delprat, G B,¹² 1916 Infant six days old Congenital atresia of third portion of duodenum Stomach and duodenum presented gross appearance of hourglass stomach *Gastro-enterostomy* Recovery

Case 3—Higgins, T T,¹³ London, 1923 Male infant one week old Biliary vomiting since birth No bowel movement after second day Emaciation Visible gastric peristalsis Roentgenograms after giving barium showed obstruction of lower duodenum with few flecks passing after 45 minutes Mass in region of pancreas Jejunum collapsed *Posterior gastro-enterostomy* Recovery

Case 4—Richter, H M,¹⁴ Chicago, 1924 Infant four days old Atresia of duodenum *Posterior gastro-enterostomy* Recovery

Case 5—Cutler, G D,¹⁵ 1924, cited by Clara Loitman Infant four days old Congenital obstruction of duodenum *Posterior gastro-enterostomy* Recovery

Case 6—Steward, M,¹⁶ London, cited by H C Cameron, 1925 Female infant On third day began vomiting bile Seen on fifth day Meconium stool Distention of the abdomen Roentgenograms showed duodenum greatly distended with barium Few flecks passed into jejunum *Posterior gastro-enterostomy* Recovery

Case 7—Bowling, R W,¹⁷ New York, 1926 Female infant Vomiting began with first nursing and continued Meconium stools Roentgenograms showed complete ob-

struction and great dilatation of the duodenum Operation on ninth day Weight 5 lbs
Duodenojejunostomy (antecolic) Recovery

Case 8—Sweet, G B, and Robertson, C,¹⁸ New Zealand, 1927 Female infant nine days old Vomiting began with lactation and persisted, becoming projectile Very little meconium Loss of weight Visible gastric peristalsis Operation on tenth day Duodenum dilated in third portion Jejunum collapsed *Anterior gastro-enterostomy* Home on ninth day Twelve days later, returned to hospital with vomiting as before *Duodenojejunostomy* performed Recovery

Case 9—Porter and Carter,¹⁹ cited by Clara Loitman 1927 Infant successfully operated upon for congenital atresia of the duodenum After four years, in perfect health Type of operation not stated

Case 10—Ladd, W E,²⁰ Boston, 1932 Hosp No A5528 Premature infant, four days old Vomiting since birth Visible epigastric peristalsis Complete retention of barium in duodenum after four hours *Posterior gastro-enterostomy* Recovery

Case 11—Ladd, W E,²⁰ Boston, 1932 Hosp No 3599 Female infant, age six days Vomiting since birth Intrinsic obstruction of duodenum *Posterior gastro-enterostomy* Recovery

Case 12—Donovan, E J,²¹ New York, 1936 Cesarean baby Biliary vomiting since birth Roentgenogram on ninth day showed obstruction at third portion of duodenum At operation obstruction seemed to be due to pressure by superior mesenteric vessels *Duodenojejunostomy* (antecolic) Three rows of suture Recovery

Case 13—Donovan, E J,²¹ New York, 1936 Male infant Seen at age of 17 days Biliary vomiting since birth Upper abdomen distended Visible epigastric peristalsis Roentgenograms show duodenum greatly dilated with small particles of barium passing after 40 minutes Duodenum as large and thick-walled as the stomach Obstruction seemed under superior mesenteric vessels *Duodenojejunostomy* (antecolic) Three rows of suture Recovery

Case 14—Morton, J J, and Jones, T B,²² Rochester, N Y, 1936 Infant four days old Vomiting began 48 hours after birth Dehydration Visible gastric peristalsis Mongolian idiot *Posterior gastro-enterostomy* Duodenum greatly dilated and walls very thin Recovery Two years later death from pneumonia Autopsy showed congenital absence of third portion of duodenum

Case 15—Morton, J J and Jones, T B,²² Rochester, N Y, 1936 Female infant Vomiting began fifth day On twelfth day, visible gastric peristalsis Roentgenograms with barium showed complete block in second part of duodenum At operation the dilated duodenum was opened longitudinally at point of obstruction and a 2 Mm-thick diaphragm removed with electric cautery Bowel closed transversely Convalescence stormy Recovery

Case 16—Tallerman, K H, and Levi, D,²³ England, 1938 Male infant, age 15 weeks Began vomiting biliary material one day after birth On sixth day roentgenogram showed obstruction in second part of duodenum At operation an *anterior gastro-enterostomy* On third day, wound was opened and a gastrostomy performed because of failure of anastomosis to function On seventeenth day, abdominal wound resutured Bile continued to leak and digest the skin Recovery after two months

COMMENT—It will be seen that up to 1918, only two cases in this group had been successful By 1928 (ten-year period), only seven had been added, and at the end of 1938, there was a total of 16 It will be noted also that in these 16 successful operations a gastro-enterostomy was performed nine times, a duodenojejunostomy five times, the duodenum was opened and a septum removed once (Morton and Jones) and in one case the type of operation was not stated I am of the opinion that in the high obstructions of the duodenum (above the ampulla of Vater) a gastro-enterostomy is the procedure of

choice In the lower obstructions, in which the degree of dilatation of the duodenum is great, a duodenojejunostomy is preferable Naturally, the technic is difficult, because one is making an opening between a dilated viscus and a jejunum which has never functioned and has the caliber of a goose-quill Under these conditions, injection of air or water into the collapsed jejunum, as advocated by Webb and Wangenstein,²⁸ may facilitate the procedure, and the employment of only two rows of suture makes it technically easier It is obvious, of course, that the employment of the finest needles and silk is essential to success

Group C In addition to the 19 successful cases in Groups A and B, there have been six others in which the obstruction was due to an abnormal band or an adhesion, and by the removal or severance of this structure the continuity of the bowel was successfully reestablished Five of these involved the duodenum and one the ileum

Case 1—Jewesbury, R C, and Page, Max,²⁴ England, 1922 Female infant Vomiting of bile since first feeding Loss of weight Roentgenogram showed obstruction between second and third portion of duodenum At operation (Mr Page) on twelfth day, the first part of jejunum was found to be twisted and fixed by adhesions which were divided Recovery

Case 2—Jackson, Reginald,²⁵ Madison, Wis, 1926 Female infant, seven days old Projectile vomiting began third day Weight 4½ lbs Barium given and partial obstruction seen in region of pylorus Next few days, vomitus contained bile At operation, on twenty-first day, a dense vascular veil was found compressing second portion of duodenum This was divided Recovery

Case 3—Carter, R F,¹¹ New York, 1933 Infant seven days old Vomiting since birth, projectile in character No abdominal distention Roentgenogram with barium showed complete occlusion of first part of duodenum At operation a fibrous band was divided and the obstruction relieved Recovery

Case 4—Davenport, G L, and Goldberg, S L,²⁶ Chicago, 1934 Premature infant Vomiting, distention, absence of stools At operation, on third day of life, loops of upper jejunum distended Obstruction caused by adhesion to parietal peritoneum in left upper quadrant Released Recovery

Case 5—Morton, J J, and Jones, T B,²² Rochester, N Y, 1936 Infant few days old Roentgenogram showed obstruction in duodenum At operation duodenum was fixed by adhesions in several places These were divided Recovery

Case 6—Stenson, Walter,²⁷ New York, 1938 Female infant, four days old (eight months premature twin) Vomiting began fourth day Barium roentgenogram showed obstruction in second part of duodenum At operation a band was divided in front of duodenum Portal vein accidentally opened Bleeding controlled by packing Convalescence stormy Recovery

To this list, I wish to add my own experience with 14 cases of congenital obstruction covering a period of the past 13 years, six involving the jejunum and ileum with a fatal result in each case, and eight involving the duodenum, four of which resulted successfully

CASE REPORTS

JEJUNUM AND ILEUM

Case 1—Infant Carey Born at Presbyterian Hospital, December 5, 1925, with abdomen greatly distended Few large peristaltic waves seen about umbilicus Barium

enema roentgenogram showed collapsed colon. On December 6, 1925, a plain roentgenogram showed great distention of loops of ileum. Operation under local anesthesia. McBurney incision. *Ileostomy*. On January 16, 1926, the ileostomy was closed, with resection and lateral anastomosis. January 22, 1926, death from peritonitis. *Autopsy*. Terminal three inches of ileum size of goose-quill.

Case 2—Infant Susie Brown (Fig 1), age two days. Cook County Hospital.

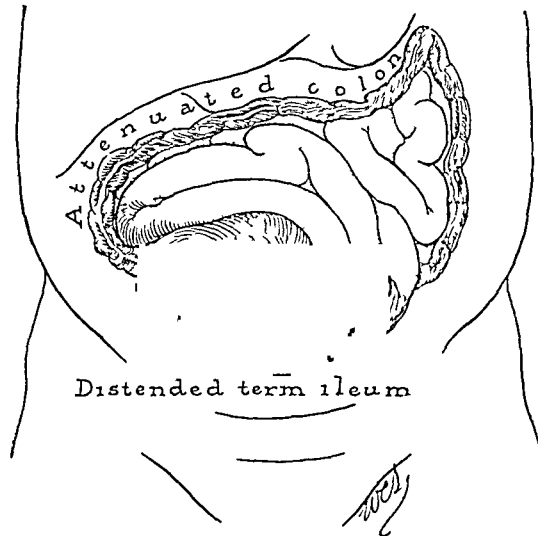


FIG 1—Case 2. Age two days. Congenital obstruction at the terminal ileum. *Ileostomy*. Death.

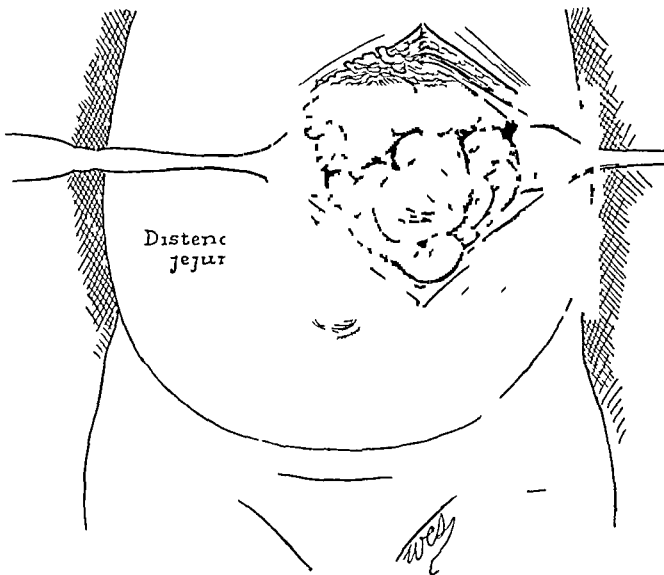


FIG 2—Case 3. Age two days. Congenital obstruction of the jejunum from adhesions. Adhesions divided. Death from pneumonia, four days after operation.

Vomiting since birth. Distention progressively more marked, involving entire abdomen. *Operation*—July 10, 1929. Entire small bowel distended, most marked at cecum. Entire colon collapsed, rudimentary in size—average diameter about 1 cm. *Ileostomy*. Content of terminal ileum thick, tenacious meconium which could not drain. Death in 24 hours.

Case 3—Infant May Jones (Fig 2), age two days. Cook County Hospital. Vomiting since birth. No bowel movement except meconium. Distention of upper abdomen.

BOWEL OBSTRUCTION IN NEW BORN

becoming progressively worse Operation—October 2, 1929 Obstruction in upper jejunum from adhesions between two loops of bowel Above distention, below collapse Adhesions divided, allowing distal loop to fill at once October 6, 1929, death from pneumonia

Case 4—Infant Heag (Fig 3), age three days Cook County Hospital Admitted January 10, 1931 Vomiting bile stained material ever since birth Marked distention of entire abdomen Operation—January 10, 1931 Ether Evidence of general peritonitis Loops of ileum greatly dilated down to point where there is complete obstruction, beyond which ileum is collapsed Six inches of bowel proximal to obstruction is black and gangrenous Lateral anastomosis, but case considered hopeless Death in 24 hours

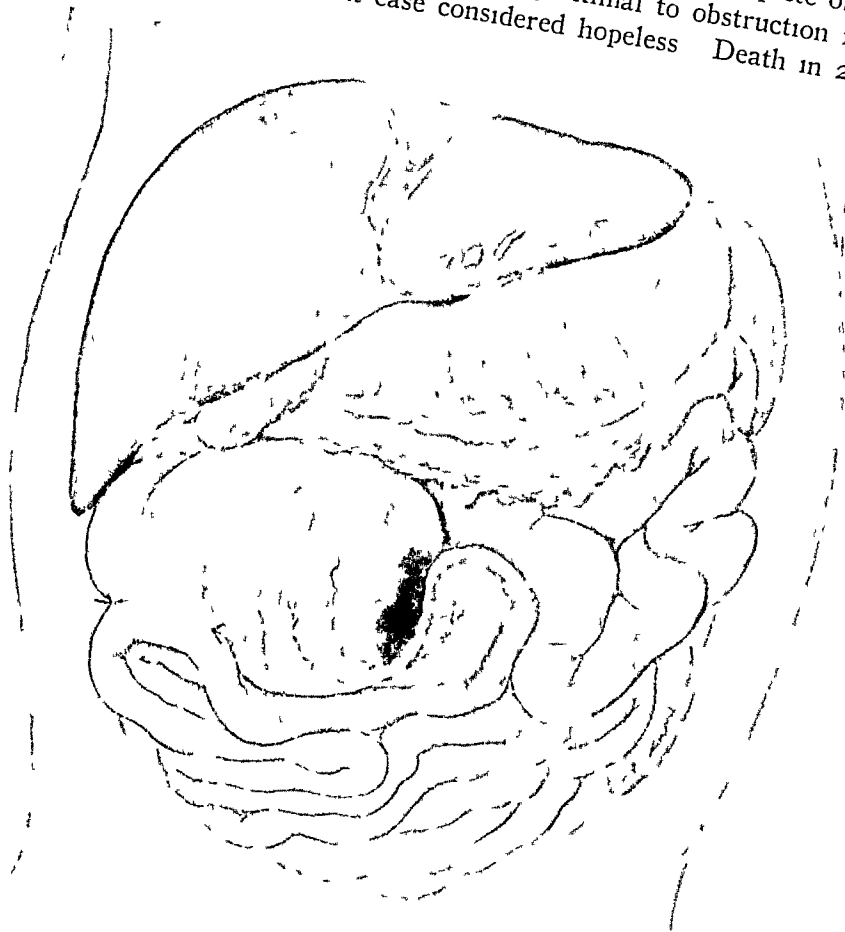


FIG 3—Case 4 Age three days Congenital atresia of the upper ileum Lateral anastomosis Death 24 hours after operation

Case 5—Infant Wisnewski (Fig 4), age one week Born at Cook County Hospital, June 8, 1931, with apparent congenital bowel obstruction Seen by Doctor Parmelee who found narrowing of rectum two inches above orifice, which was considered cause of the obstruction Operation—June 10, 1931 Sigmoidostomy Colon empty Vomiting continued Soon apparent that obstruction must be higher Second Operation—June 15, 1931 Small bowel obstruction about 15 ins above ileocecal valve Above this great dilatation, below bowel collapsed Lateral anastomosis Death June 16, 1931 No autopsy

Case 6—Infant Peter DeFrancisco (Fig 5), age six days Born January 15, 1935 at Cook County Hospital Weight 5 lbs, 12 oz Vomiting since birth Nothing per rectum Great distention of abdomen and tympany Dehydration Enema and blocked tube three inches up Loss of weight Operation—January 21, 1935 Complete obstruction

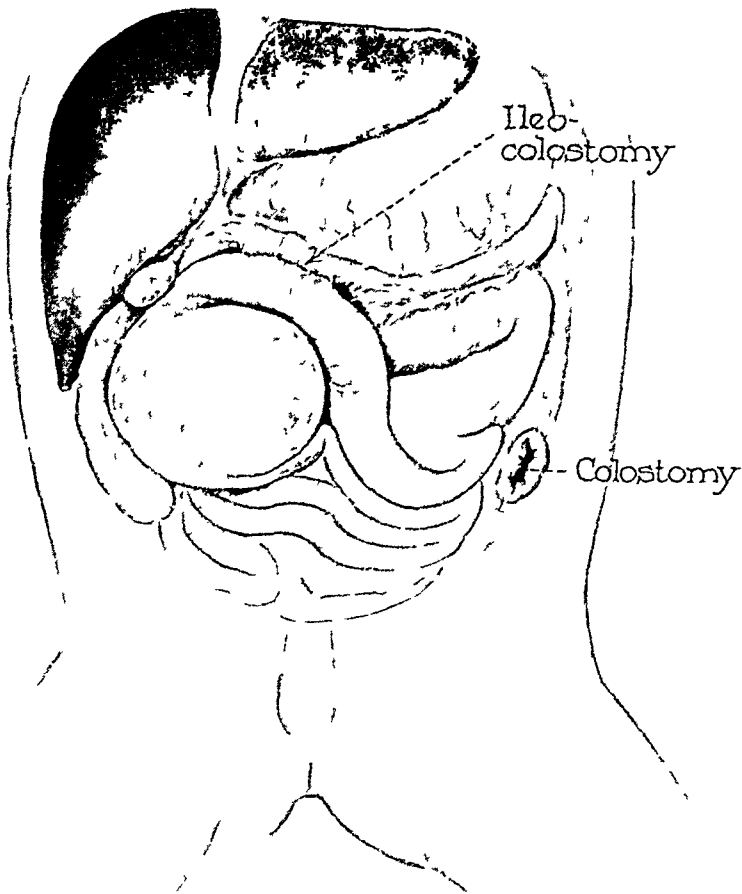


FIG. 4—Case 5. Age one week. Congenital atresia of the upper ileum plus an imperforate anus. Lateral anastomosis after sigmoidostomy. Death.

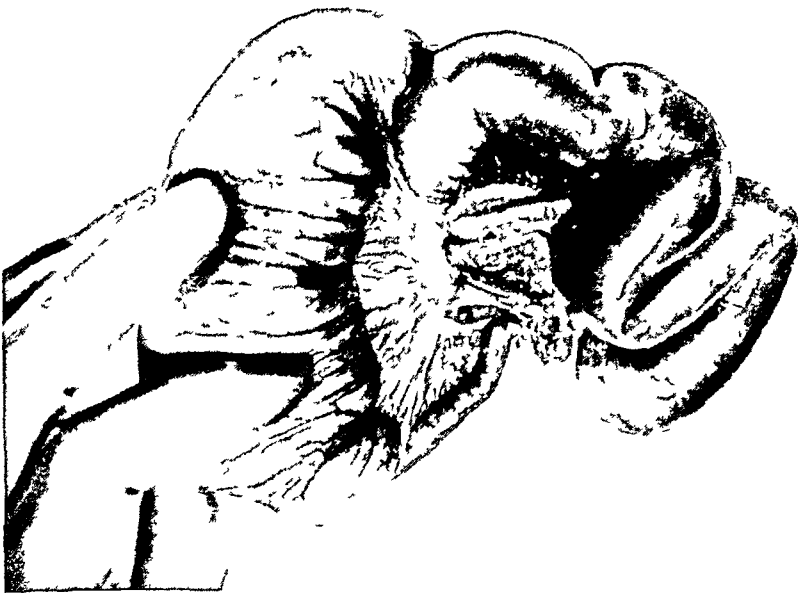


FIG. 5—Case 6. Age six days. Congenital obstruction of the midileum. Lateral anastomosis. Death from pneumonia 24 hours after operation.

BOWEL OBSTRUCTION IN NEW BORN

tion of midportion of ileum Bowel above 6 cm wide, below 6 Mm wide Deflation with needle *Lateral anastomosis* Death January 22, 1935 *Autopsy* Atresia at junction and middle one-third Bronchopneumonia

DUODENUM

Case 7—Chiuso, Rose (Fig 6), Mongolian, age three weeks Birth at Presbyterian Hospital Weight 7 lbs, 2 oz Admitted to Presbyterian August 18, 1930 Two days after infant was brought home from hospital, she began vomiting projectily after every

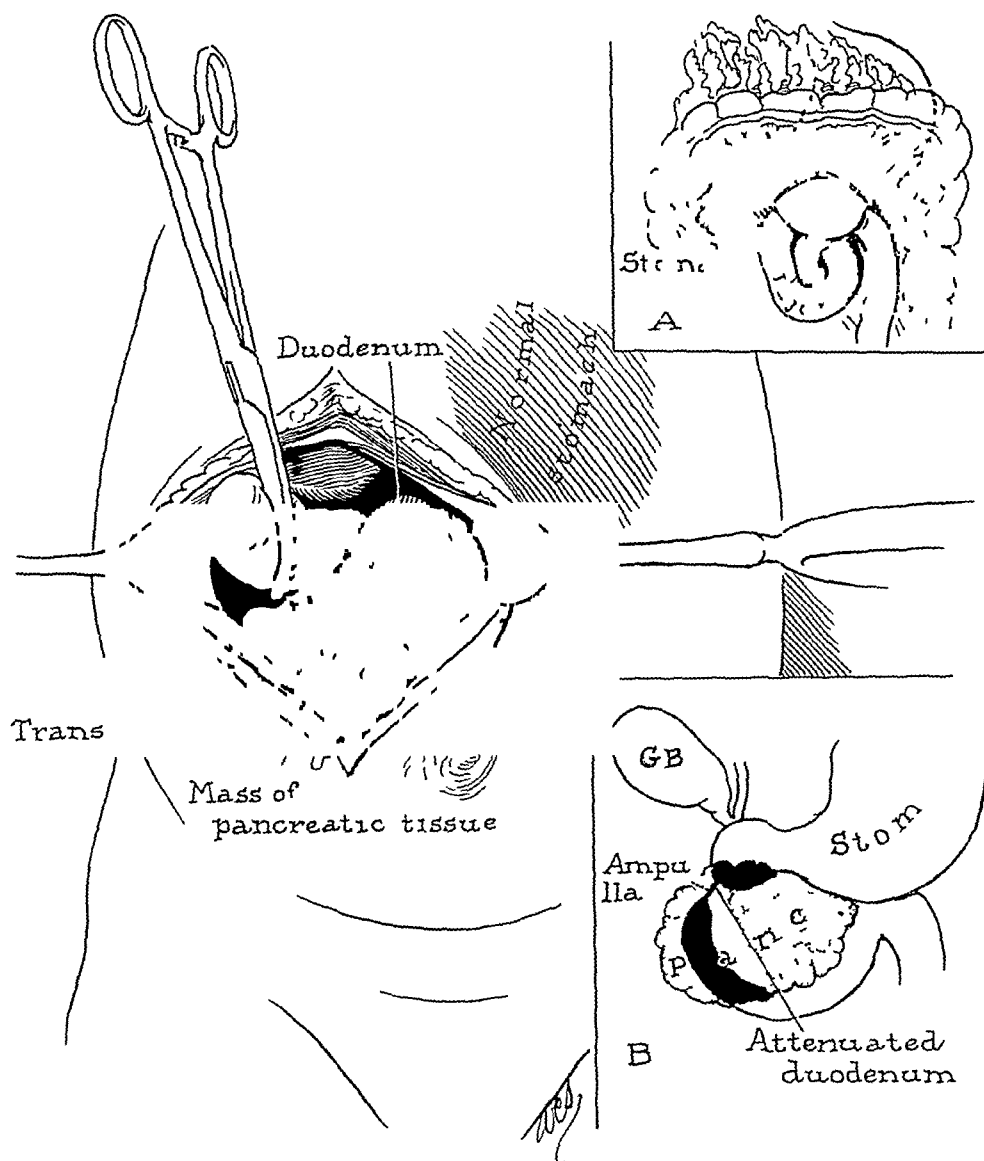


FIG 6—Case 7 Age three weeks Congenital atresia of the duodenum Posterior gastro-enterostomy Recovery Death from pneumonia five weeks later

feeding Dehydration Visible epigastric peristalsis Small tumor mass palpable in right upper quadrant Pustule in right inguinal region Vomitus bile stained Peristaltic waves *Operation*—August 20, 1930 Local anesthesia Rectus incision No pyloric tumor Beyond first 2½ inches of duodenum it could not be followed Merely pancreas in view Below pancreas duodenum again seen as far as upper margin of transverse colon *Posterior gastro-enterostomy* performed because of evident atresia in region of ampulla of Vater Three-row method with one clamp on both stomach and jejunum Postoperative course uneventful Recovery One month later, developed pneumonia and died September 24, 1930 *Autopsy* Gastro-enterostomy patent with no leak An atresia of the duodenum 14 Mm long, in center of which the ampulla of Vater opened

Case 8—Ross, Marion (Fig 7) Born February 25, 1931 Weight 8½ lbs Soon after birth, began projectile vomiting and did not take food well Roentgenograms at first showed no opening at pylorus, but later, a little barium passed into small bowel Diagnosis made of congenital pyloric stenosis, after failure to obtain relief of vomiting by atropine or luminal Diagnosis confirmed by Doctor Grulee, who thought he could feel a pyloric tumor Once or twice, a small amount of bile was noticed in the material vomited *First Operation*—March 11, 1931 Infant was 16 days old Weight 6½ lbs Right rectus incision under local anesthesia Pylorus normal First two inches of duodenum wider than normal and could not be followed further Abdomen closed Vomiting continued *Second Operation*—March 13, 1931 Under ether anesthesia Left paramedian incision *Posterior gastro-enterostomy* Postoperative course uneventful after first few days Recovery



FIG 7—Case 8 Age nine Congenital atresia of the second portion of the duodenum Posterior gastro enterostomy performed at age of two weeks Excellent health eight years later

Case 9—Olson, Richard, age four days Admitted to Presbyterian Hospital June 28, 1931 Infant born at home three days previously, apparently normal Mongolian type Biliary vomiting for past three days Visible peristalsis Condition poor *Operation*—June 29, 1931 Stomach and duodenum distended with gas Jejunum collapsed *Posterior gastro-enterostomy* No clamp used Diagnosis congenital atresia of third portion of duodenum probably just below ampulla of Vater Death on following day No autopsy

Case 10—Wilder, Frank (Fig 8), age seven years July 26, 1931, admitted to Cook County Hospital Abdominal

pain Inability to pass gas per rectum for 38 hours Vomiting for two hours When he was a baby had a Ramstedt operation for congenital pyloric stenosis Since then he has had many attacks of what appeared to be partial intestinal obstruction, each lasting from two days to three weeks Present attack began 38 hours ago with pain over entire abdomen, localized chiefly in umbilical region, associated with vomiting and inability to pass gas July 27, 1931, discharged from hospital much relieved

November 5, 1931, readmitted to hospital, complaining of cramp-like, intense pain for 13 hours Vomiting for eight hours Examination General tenderness, distention November 6, 1931, vomiting persisting *Operation*—Right rectus incision There had been complete failure of rotation of intestine so that all of small bowel lay in front of colon No retroperitoneal duodenum Volvulus of midgut on axis of superior mesentery artery causing obstruction at duodenojejunal junction Bowel had become more or less fixed in this position by adhesions Veins greatly distended Lymph nodes enlarged Cecum lay near midline above umbilicus Adhesions divided, permitting rotation of bowel back to normal position December 22, 1931, discharged Follow-Up Seen in Clinic June 28, 1932, January 28, 1938, and January 10, 1939, appeared to be in perfect health since operation (Fig 9)

Case 11—Schmidt, Phyllis (Fig 10), age five months Born June 20, 1935 Weight 5 lbs Cook County Hospital November 20, 1935, admitted to hospital Weight 12 lbs, 11 oz History of vomiting more or less since birth Nose, lips, hands and feet always blue

Examination (1) Congenital heart (2) Vomiting of bloody material Stools posi-

BOWEL OBSTRUCTION IN NEW BORN

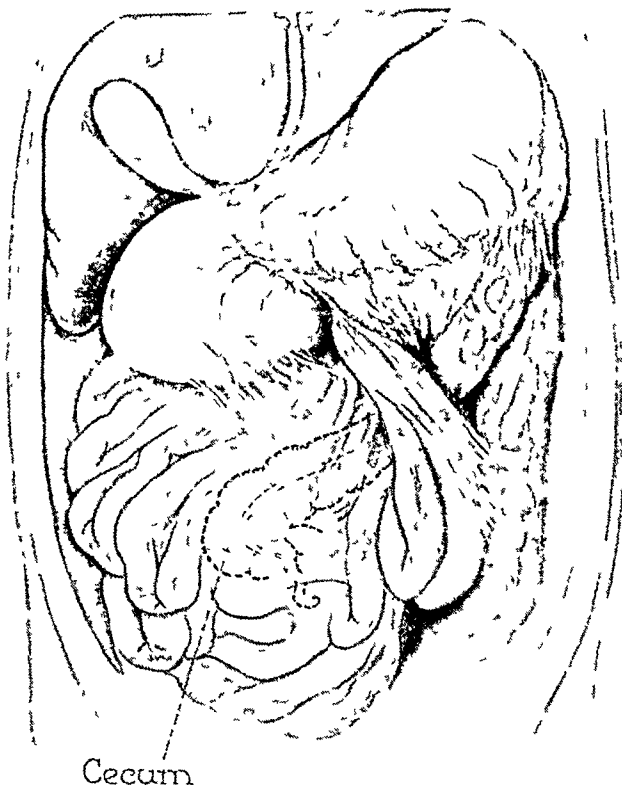


FIG 8—Case 10 Age seven Complete obstruction at the duodenojejunal angle following repeated attacks of partial obstruction since infancy Pathology Volvulus of midgut and incomplete rotation of the colon Operation Adhesions freed and volvulus untwisted Recovery Excellent health seven years later

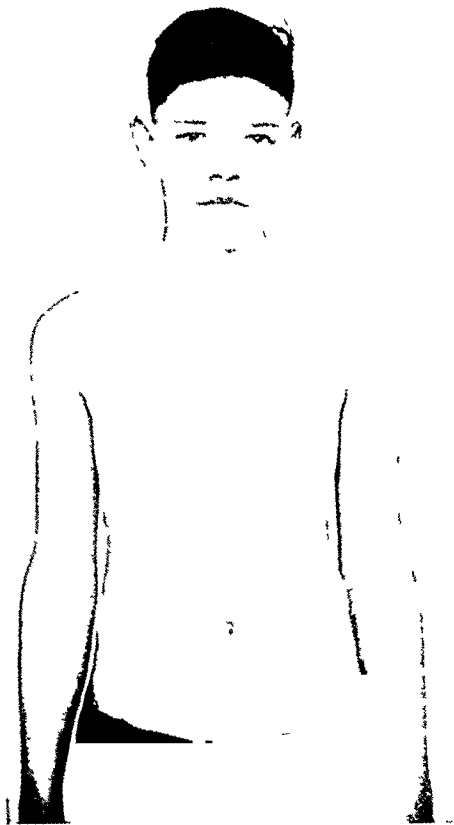


FIG 9—Case 10 Operated upon in 1931, seven years ago, for chronic obstruction at the junction of the duodenum and jejunum, due to rotation of the small bowel on the axis of the superior mesenteric artery

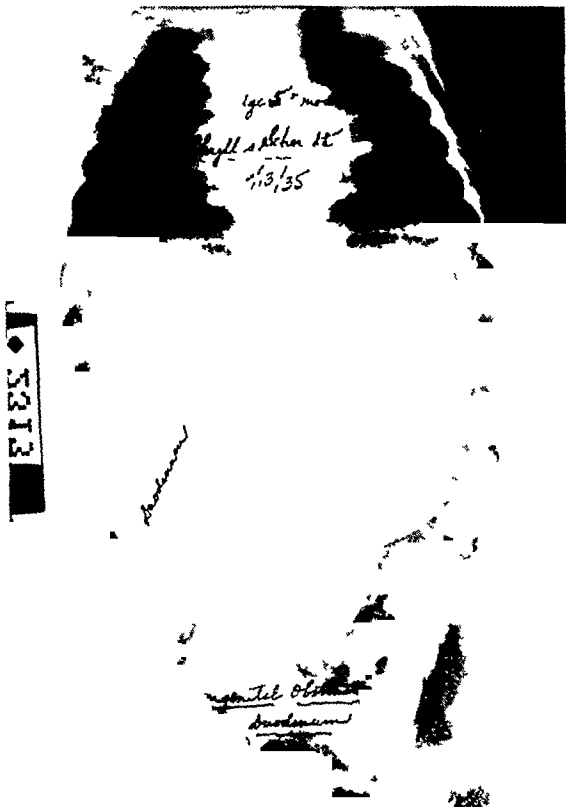


FIG 10—Case 11 Age five months Congenital partial obstruction of the duodenum Duodenojejunosomy Death from pneumonia

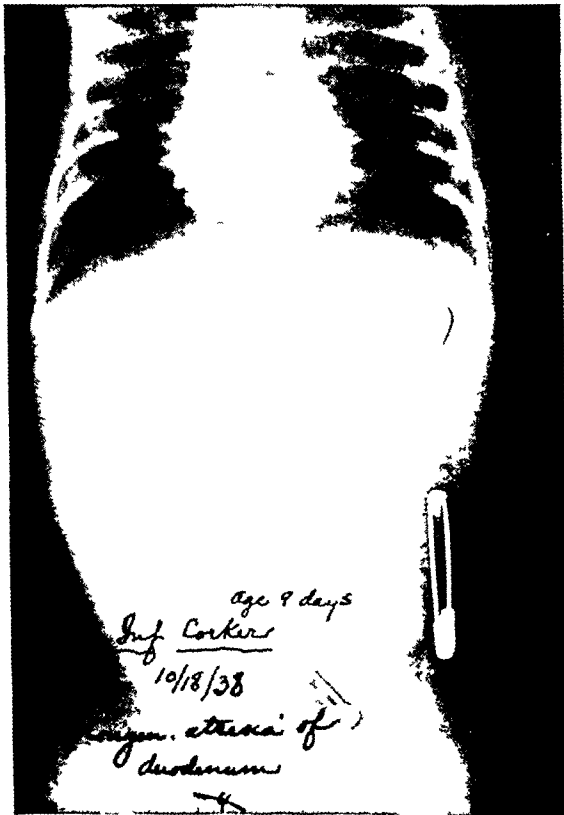


FIG 11—Case 13 Age nine days Congenital obstruction of the third part of duodenum Duodenojejunosomy (antecolic) Entero enterosomy Recovery

tive for blood (3) Cough and fever Temperature 100° - 101° F December 13, 1935, barium by mouth Roentgenograms showed that the barium began to leave stomach after two hours and emptied into a huge, dilated duodenum Operation—December 16, 1935 Baby has cough and fever 102° F Right rectus incision Huge dilatation of stomach and duodenum appearing almost like an hour-glass stomach Deflated by needle

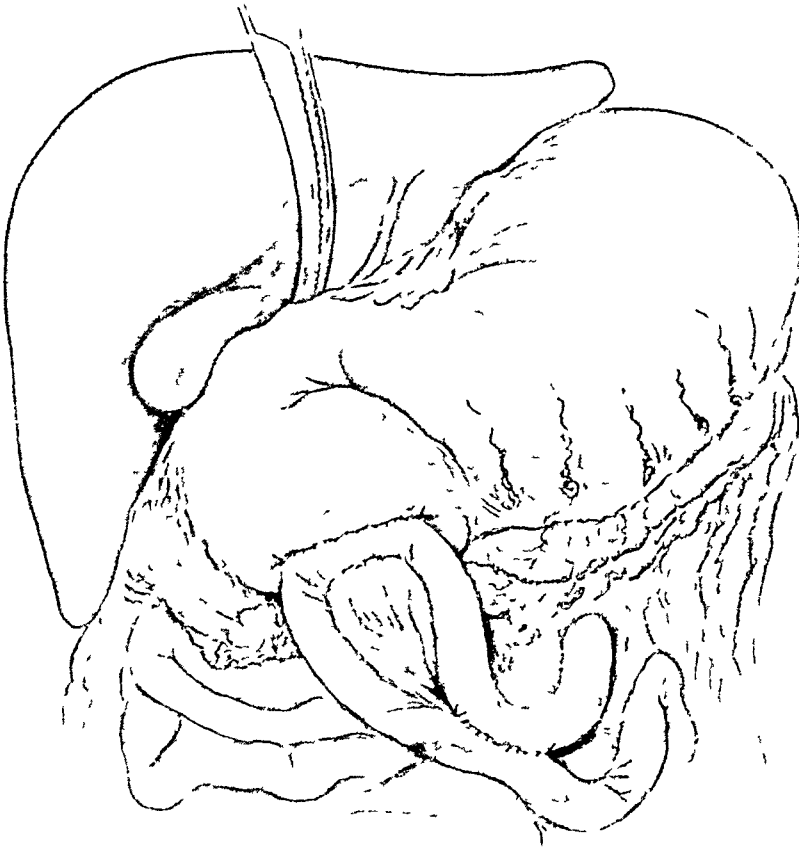


FIG 12—Case 13 Congenital obstruction of the third part of the duodenum Duodenojejunostomy (antecolic) Entero enterostomy Recovery



FIG 13—Case 13 Age six months Congenital obstruction of the third part of the duodenum Duodenojejunostomy plus entero enterostomy Recovery Excellent health six months later

and syringe through wall of stomach Duodenojejunostomy December 17, 1935, death Temperature 106° F Pneumonia

Case 12—Mowcra, John, age five days Birth normal, May 25, 1938 On second day began biliary vomiting Jaundice Obstipation Physiologic icterus Roentgenogram after barium showed none passed beyond dilated duodenum in seven hours Opera-

BOWEL OBSTRUCTION IN NEW BORN

tion—June 3, 1938 Duodenum dilated down to crossing of superior mesenteric vessels Jejunum collapsed *Posterior gastro-enterostomy* June 13, 1938, death *Autopsy* (1) Bronchopneumonia—all lobes (2) Icterus—neonatorum (3) Incomplete rotation of colon (4) Patent foramen ovale

Case 13—Infant Corker (Fig 11), age nine Normal birth at Cook County Hospital, October 9, 1938 Weight 5 lbs, 6 oz Breast fed On second day, began vomiting a chocolate colored, bloody material Weight 4 lbs, 4 oz Convulsion From fifth day, after every nursing, biliary vomiting No tumor palpable October



FIG 14—Case 14 Age eight days Congenital obstruction of the third part of the duodenum Duodenojejunostomy (transmesocolic) Recovery Excellent health four months after operation

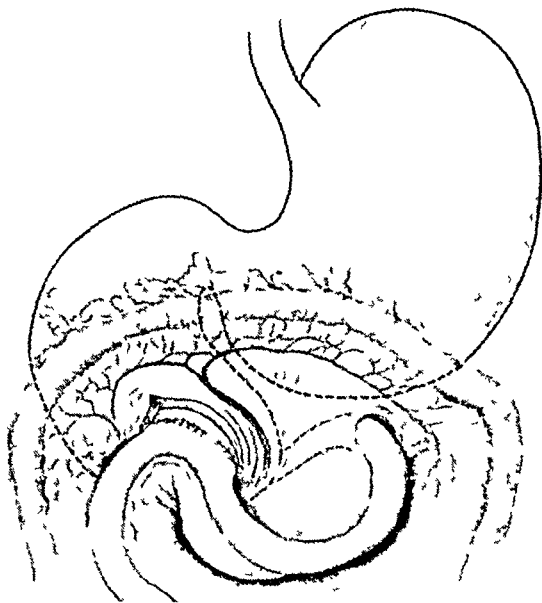


FIG 15—Case 14 Age eight days Congenital obstruction of the third part of the duodenum Duodenojejunostomy (transmesocolic) Recovery Excellent health four months after operation

17, 1938, barium meal roentgenogram showed complete obstruction at third part of duodenum, with dilatation Few flecks of barium passed after three hours *Operation*—October 18, 1938, Local anesthesia Duodenum dilated, 2 cm wide, down to crossing of



FIG 16—Case 14 Age eight days Congenital obstruction of the third part of the duodenum Duodenojejunostomy (transmesocolic) Recovery Excellent health four months after operation

superior mesenteric vessels Jejunum size of goose-quill *Antecolic duodenojejunostomy* plus *entero-enterostomy* Fine silk, two-row method No clamps Recovery (Figs 12 and 13)

Case 14—Infant Manuel (Fig 14) Born at Cook County Hospital, December 2, 599

1938 Weight 7 lbs Biliary vomiting since birth Dehydration December 8, 1938, weight 5 lbs, 8 oz Visible epigastric peristalsis Barium meal, December 9, 1938, showed complete obstruction of lower duodenum, with dilatation Nothing passed after two hours *Operation*—December 10, 1939 (age eight days) Local anesthesia Rectus incision. Dilated duodenum down to crossing of mesenteric vessels Jejunum collapsed *Duodenojejunostomy* (transcolic) Silk, two rows Recovery (Figs 15 and 16)

CONCLUSIONS

(1) Progress in this field of surgery depends largely on the early diagnosis of the obstructive lesion and adequate preoperative preparation

(2) The use of local anesthesia is strongly advised

(3) If the atresia is in the jejunum or ileum simple enterostomy is useless Adequate exposure and a short-circuiting lateral anastomosis offers the only hope of success

(4) If the obstruction involves the duodenum, a gastro-enterostomy for those above the ampulla and a duodenojejunostomy for those below the ampulla are the procedures of choice The addition of an entero-enterostomy between the afferent and efferent loops of the anastomosis, where there has been narrowing at the proximal end of the suture line (as in my Case 13), may make the difference between success and failure

(5) Much depends upon the technical skill of the surgeon, and the use of the finest suture material is essential

(6) All of these little patients demand the most painstaking postoperative care

REFERENCES

- ¹ Calder Two Examples of Children Born with Preternatural Conformation of the Guts Med Essays, Edinburgh, 1, 203, 1733
- ² Theremin, E. Über Cong. Occlus. des dunndarms Deutsch Ztschr f Chir, 8, 34, 1877
- ³ Tandler, J. Zur Entwicklungs geschichte des Menschlichen Duod. in frühen Embryonalstadien Morph Jahrb, 29, 187, 1902
- ⁴ Davis, D. L., and Poynter, C. W. M. Congenital Occlusions of the Intestines with Report of Case of Multiple Atresia of the Jejunum Surg, Gynec, and Obstet, 34, 35, 1922
- ⁵ Bland-Sutton Imperforate Ileum Am Jour Med Sci, 98, 457, 1889
- ⁶ Fockens, P. Ein operativ geheilter Fall von Kongenitale Dunndarm Atresia Zentralbl f chir, 38, 532, 1911
- ⁷ Ernst, N. P. A Case of Congenital Atresia of the Duodenum Treated Successfully by Operation Brit Med Jour, 1, 644, 1916
- ⁸ Seidlin, S. M. Congenital Duodenal Septum with Obstruction Bull Johns Hopkins Hosp, 37, 328, November, 1925
- ⁹ Garvin, J. A. Congenital Occlusion of the Duodenum by a Complete Diaphragm Am Jour Dis Child, 35, 109, January, 1928
- ¹⁰ Demmer, Fritz. Atresie Ilei—Resectio ileo-caecalis-Heilung Arch f klin Chir, 147, 471, 1927
- ¹¹ Carter, R. F. Congenital Occlusion of the Duodenum and Small Intestine A Clinical Consideration with Report of Two Successful Cases Jour Ped, 2, 27, 1933
- ¹² Weeks, A., and Delprat, G. B. Congenital Intestinal Obstruction Atresia of Jejunum Surg Clin N Amer, October, 1927
- ¹ Higgins, T. T. Subacute Pancreatitis Occurring in Association with Acute Intestinal Obstruction in a Newborn Infant Brit Jour Surg, 11, 592, 1923-1924

BOWEL OBSTRUCTION IN NEW BORN

- ¹⁴ Richter, H M Abt's Pediatrics, W B Saunders, Phila , 3, 512, 1924
- ¹⁵ Cutler, G D Cited by Clara Loitman Congenital Occlusion of the Intestine Boston Med and Surg Jour , 197, 21, July, 1927
- ¹⁶ Steward, M Cited by H C Cameron Brit Med Jour , 1, 768, April 25, 1925
- ¹⁷ Bowling, R W Complete Congenital Obstruction of Duodenum Duodeno-jejunostomy at Nine Days Trans New York Surg Soc , ANNALS OF SURGERY, 83, 543, 1926
- ¹⁸ Sweet, G B, and Robertson, C A Case of Congenital Atresia of the Jejunum with Recovery Arch Dis Child, New Zealand, 2, 186, 1927
- ¹⁹ Porter and Carter Cited by Clara Loitman Congenital Occlusion of the Intestine Boston Med and Surg Jour , 197, 21, July, 1927
- ²⁰ Ladd, W E Congenital Obstruction of the Duodenum in Children New England Jour Med , 206, 277, 1932
- ²¹ Donovan, E J Congenital Atresia of the Duodenum in the Newborn ANNALS OF SURGERY, 103, 455, March, 1936
- ²² Morton, J J, and Jones, T B Obstruction About the Mesentery in Infants ANNALS OF SURGERY, 104, 864, 1936
- ²³ Tallerman, K H, and Levi, D Duodenal Atresia Gastro-Enterostomy—Recovery Proc Royal Soc Med , 31, 761, May, 1938
- ²⁴ Jewesbury, R C, and Page, Max Two Cases of Duodenal Obstruction in Infants Treated by Operation Successfully Proc Royal College of Med , 16, 1922-1923
- ²⁵ Jackson, Reginald Congenital Constriction of Duodenum Due to an Abnormal Fold of the Anterior Mesogastrium ANNALS OF SURGERY, 84, 723, November, 1926
- ²⁶ Davenport, G L, and Goldberg, S L Illinois Med Jour , 66, 563, December, 1934
- ²⁷ Stenson, Walter Duodenal Occlusion in the Newborn Am Jour Dis Child 56, 1066, November, 1938
- ²⁸ Webb, C H, and Wangenstein, O H Congenital Intestinal Atresia Am Jour Dis Child , 41, 262, 1931

DISCUSSION—DR WILLIAM E LADD (Boston) We are indebted to Doctor Miller for emphasizing the point that early diagnosis is at least one of the main factors for lowering the mortality in the future of these conditions

We have been much interested in the subject of this paper for a number of years at the Children's Hospital, where we have had a moderately large experience with abdominal surgery of small infants, including over 700 cases of congenital pyloric stenosis and 116 cases of various types of congenital obstruction of the small bowel

It surprises me that Doctor Miller should have had more cases of intrinsic obstruction of the duodenum than of extrinsic obstruction due to faults of rotation, which have been far more common in our clinic Doctor Miller states that the clinical picture often simulates that of pyloric stenosis I do not recall that a differentiation between these two conditions has been a matter of difficulty In the atresia patients the vomiting starts with the first feedings and the patient, unless relieved surgically, would be dead before the usual time for the symptoms of pyloric stenosis to start In the midgut volvulus patients, the symptoms are those of acute intestinal obstruction rather than those of starvation presented by the pyloric stenosis patient It is only, then, in the duodenal stenosis case or the partial extrinsic obstruction that confusion might arise In the case of pyloric stenosis the tumor can always be felt if the patient is properly examined, while bilious vomiting is in favor of duodenal obstruction as Doctor Miller has mentioned The roentgenogram without the use of contrast media will give a definite diagnosis in the patients with complete obstruction Barium may be used in the patients with partial obstruction

For intrinsic atresia of the duodenum, duodenojejunostomy is a preferable operation to gastrojejunostomy, for two reasons First, it drains the duo-

denum better. Second, it prevents neutralization of the acid secretion of the stomach, and consequent loss of appetite. This proved very trying in one of our cases of gastrojejunostomy and was relieved only after a supplementary duodenojejunostomy had been performed. In stenosis of the duodenum the choice of operation is less important.

For cases of extrinsic duodenal obstruction due to faulty rotation, the operation first described by me, in 1932, and by Morton, in 1936, is the only operation which has proved satisfactory in our hands. There are three essential features to this operation. First, delivery of the whole midgut outside the abdomen, second, untwisting the volvulus when present (it has been present in most of our cases), and third, exposure of the duodenum through its whole course.

Much progress has been made in the last ten years. The prognosis depends on the condition of the patient, the condition of the bowel (whether there is necrosis or perforation), the skill of the surgeon, and the pre- and postoperative care. When Doctor Miller states that only three cases of jejunal or ileal atresia had been successfully operated upon, he must have overlooked some of the literature. In 1933, I reported three cases of my own successfully operated upon, and four from the literature. Since that time, we have had three more successful anastomoses for jejunal and ileal atresia. Again, Doctor Miller states that there have been only 16 cases of successful anastomosis for intrinsic duodenal obstruction. As I reported seven cases of duodenal anastomosis successfully operated upon at the Children's Hospital prior to 1937, which he has not mentioned, he must have missed this article, also. When Doctor Miller mentions that there have been only six cases of extrinsic duodenal obstruction relieved by operation, it is quite surprising.

TABLE I

CONGENITAL INTRINSIC OBSTRUCTION OF DUODENUM

Operation	Number of Cases	Recov- eries	Deaths
Jejunostomy (for feeding)	1	0	1
Posterior gastro-enterostomy	2	1	1
Duodenojejunostomy	14	7	7
	—	—	—
Total	17	8	9

CONGENITAL EXTRINSIC OBSTRUCTION OF DUODENUM

Ladd's operation	29	24	5
	—	—	—
Total both types	46	32	14

In the extrinsic type of obstruction there were four additional cases which had various other types of operation which were unsuccessful.

Morton reported nine cases in 1936. I reported 19 in 1937, and Donovan 12 in January, 1939. At the present time at the Children's Hospital, we have had six cases successfully operated upon for jejunal or ileal atresia, nine for intrinsic duodenal obstruction, and 24 for extrinsic duodenal obstruction. Although the mortality is still higher than it should be, the picture is not quite so gloomy as Doctor Miller paints it, and I think the mortality should be very much lower in the next few years than it has been in the past.

Doctor Ladd then showed several slides demonstrating the following conditions:

A case of duodenal stenosis resulting from an intrinsic obstruction of the

third part of the duodenum, in which the duodenum was almost as large as the stomach

A case of partial obstruction due to malrotation of the gut with a volvulus of about 90° , which was not sufficient to interfere with the circulation. Many of them had twisted more than one complete circle, and he recalled one which appeared to have had four complete turns. This was relieved by the operation which he had described, namely, of first untwisting the volvulus and then transferring the whole gut to the left side, exposing the duodenum throughout its whole course, which allows passage of food through the duodenum. He felt that this was an essential part of the operation for malrotation. The cases that had been operated upon by simply untwisting the volvulus have either all recurred or died. In other words, if one omits this part of the operation it is not successful.

A case of duodenal atresia in which the diagnosis was made without employing barium. With the stomach and duodenum so clearly demonstrated, plus not finding any cornified epithelium in the meconium, the diagnosis is absolutely positive, or as positive as any diagnosis ever is. This was relieved successfully by duodenojejunostomy.

The last case demonstrated was that of a three-day old infant who had vomiting from the first feeding. The plain film showed air in the stomach and also in a loop of bowel below. This was so confusing we took another film with the patient upside down, in the hopes that this would clarify the situation. Instead of clarifying it, however, it made it a little bit more confusing. This case was an atresia of the jejunum with an inadequate, and unattached mesentery, so that the air which was seen away down in the pelvis in the inverted position is the same air that was seen in the usual position of the stomach in the upright position. At operation, the blind end was beginning to become necrotic. About six or eight inches of the jejunum was resected, and a lateral anastomosis performed. The child had an uninterrupted convalescence and was discharged from the hospital on the fourteenth day.

DR EDWARD J. DONOVAN (New York) We have been interested in this subject for a number of years, and in January of this year, Doctor McIntosh and I reported 20 cases of congenital duodenal obstruction from the Babies' Hospital in New York. Since that time I have operated upon five additional cases. The youngest child in this first group was 30 hours old, in whom we found a volvulus of the small intestine with complete gangrene of the jejunum at that point, and nothing, of course, could be done.

In the five cases operated upon since this first group was reported, we have found some very interesting conditions. The first patient was operated upon at the age of 24 hours. This baby was born with abdominal distention, had bilious vomiting almost immediately, and continuously after the cord was tied, passed no meconium in 24 hours. At operation it was found that he had a volvulus of the small intestine with gangrene and perforation of the jejunum, a process that I would think probably had been going on about two or three days.

One other case of this five, we found had an intrinsic lesion of the duodenum. We found also that the stomach was on the right side, the duodenum on the left, the liver was in normal position. The common bile duct passed into the stomach through the posterior gastric wall. This baby was operated upon at the age of five days, and died seven days later from aspiration pneumonia.

In one other case of this five, we had given barium for diagnosis and found

at operation a volvulus of the jejunum and also found that the barium had perforated the volvulus. Therefore, I would like also to call attention to the fact that it is very important to be careful about giving these babies barium. I think Doctor Ladd's suggestion that you can get almost as much information by a plain roentgenogram of the abdomen is very helpful. It was necessary in this baby to resect the intestine, and the child died.

We have had a great many cases of volvulus of the small intestine in the series reported, and we feel the volvulus occurs because the cecum and ascending colon have not attached themselves to the posterior abdominal wall. The last stage of rotation is fixation of the ascending colon in the right lower abdomen. If fixation does not take place, it leaves everything free to turn around the superior mesenteric artery. We also attach the cecum and ascending colon to the right lower quadrant at operation believing that this prevents recurrence of the volvulus.

Doctor Donovan then showed lantern slides demonstrating other causes of congenital duodenal obstruction such as intrinsic lesions, volvulus and fixation of the duodenum in abnormal positions. He also showed slides of a case with complete reversal of rotation and duodenal obstruction.

DR J. SHELTON HORSLEY (Richmond, Va.) Doubtless many infants die from this disease because it is unrecognized. I have had three cases of congenital occlusion of the duodenum, all of them operated upon within the first seven days. Two of these cases were reported in the Virginia Medical Monthly for June, 1935. In two of them a posterior gastro-enterostomy was performed. In the other, a duodenojejunostomy was performed. One recovered and is now well, one died of pneumonia, and one of shock four hours after operation. The diagnosis between congenital pyloric stenosis and occlusion has been clearly explained by Doctors Miller and Ladd.

So far as I know, these cases are the only ones that have been reported of operation for congenital, complete atresia of the duodenum in the State of Virginia, and all of them came from one town, Newport News, where there are some excellent pediatricians. It is not at all probable that they are the only cases of this kind in Virginia. The fact is that, in all human probability, many of these cases are simply treated for improper feeding, the formula changed, and they die. The mortality from this lesion must be very considerable.

As Doctor Miller has insisted, the sutures must be of fine material. It is quite different from operating upon an adult. The tissues are very thin, and if the transverse colon is lifted up, the mesocolon is transparent and can be almost disregarded, as long as the vessels are not injured. Two tractor sutures of fine silk are placed between the jejunum and the stomach, and are held taut without any clamps on the wound, because they are unnecessary, are in the way, and there is practically no chance of infection from the stomach or upper jejunum in an infant that young. An incision is made half an inch long, and the posterior margin of the stomach is sutured to the posterior margin in the jejunum with a continuous suture of fine silk. That is continued anteriorly and tied to the original end. Anteriorly another row of sutures is placed, that is all that is necessary.

DR PHILEMON E. TRUESDALE (Fall River, Mass.) It is my feeling that Doctors Miller and Ladd and a few others merit the highest commendation for the work which they have done in this field. My interest was aroused during a visit to Cook County Hospital, Chicago six months ago. I saw Doctor Miller's cases in the convalescent stage. He showed me the records of seven cases upon which he operated successfully.

BOWEL OBSTRUCTION IN NEW BORN

On November 8, 1938, an infant one month old, weighing four pounds and ten ounces, was admitted to our hospital. It was said that the birth weight was three pounds. Vomiting, which occurred daily since birth, became more frequent. The infant was anemic, emaciated, and dehydrated. An effort was made to establish a fluid balance, 20 cc of citiated blood in normal salt solution were given intravenously. A roentgenogram demonstrated the point of obstruction to be in the transverse portion of the duodenum. After a period of preparation on behalf of the patient, on November 16, a duodenojejunostomy without the use of clamps was performed. My chief difficulty during the operation was from hemorrhage. It seemed to me that my hemostasis should have been better, and I was surprised that the little patient survived the operation. To expediate the operation some form of tiny intestinal clamp might be employed.

Last night Doctor Wilkie and I improvised a pair of miniature clamps which we describe as the hairpin clamp. It is made of two ordinary hairpins of the "bobby" type. The two pins are fastened side by side with a ligature of silk, and are held in position by a small hemostat attached across the blunt ends of both hairpins. As the pin is constructed, the outer phalange has a slight but sufficient amount of pressure to control bleeding. The parts of the clamp are simple to assemble, easy to improvise, and very useful in conserving the blood volume for these feeble infants.

DR EDWIN M. MILLER (Chicago) I do not want to prolong this discussion unnecessarily but I do wish to thank those who have taken an interest in discussing this paper. I also want to apologize to anybody anywhere if I have inadvertently overlooked some article they have written on this subject.

I have read very carefully, not only once but several times, the articles of Doctor Ladd published in 1932 and 1937, and I have picked out from those in which he has given details of the cases, the ones which I was sure, without any question of doubt, were cases of complete obstruction, operated upon a few days after birth. We all know there have been a large number of cases reported in the literature of partial obstruction, and I have not attempted, of course, to include those in this series.

PEPTIC ULCERS PERFORATING INTO THE PANCREAS *

J. SHELTON HORSLEY, M.D.

RICHMOND, VA

FROM THE SURGICAL DEPARTMENT OF ST. ELIZABETH'S HOSPITAL, RICHMOND, VA

THE STATUS of peptic ulcer of the duodenum has changed within the last 20 years. Formerly, a peptic ulcer anywhere was often considered to be a surgical lesion, and operations, especially posterior gastro-enterostomy, were the routine therapy. Lewisohn reported recurrent ulcers, usually jejunal ulcers, in about 34 per cent of the cases of gastro-enterostomy from the clinic with which he was associated. Church and Hinton found in a study of peptic ulcer that after gastro-enterostomy there were numerous complaints, only 37 per cent of the patients were free from symptoms, and 16.4 per cent had marginal ulcers. It is now fairly generally agreed among surgeons who have had much experience in gastric surgery that about 80 per cent of *duodenal* peptic ulcers may be cured by proper medical treatment. It has been established that medical treatment consists not only in diet and the administration of alkalis, but in lessening worry and nervous tension, for peptic ulcers are frequently found in high-strung, nervous individuals, although occasionally they occur in the phlegmatic. They have been found in infants.

The cases operated upon are what might be termed residual cases of duodenal peptic ulcer that resist medical treatment or that develop some complication as perforation, repeated or massive hemorrhage, or obstruction.

Gastric peptic ulcers, however, are in another therapeutic class, because in a definite proportion of gastric peptic ulcers cancer develops, and even if the ulcer is cured the scar may remain a point of irritation.

A peptic ulcer that has perforated into the pancreas presents quite a different clinical and pathologic picture from an ulcer that has not so perforated. It always gives a history of previous gastric disturbance, which may be long or short.

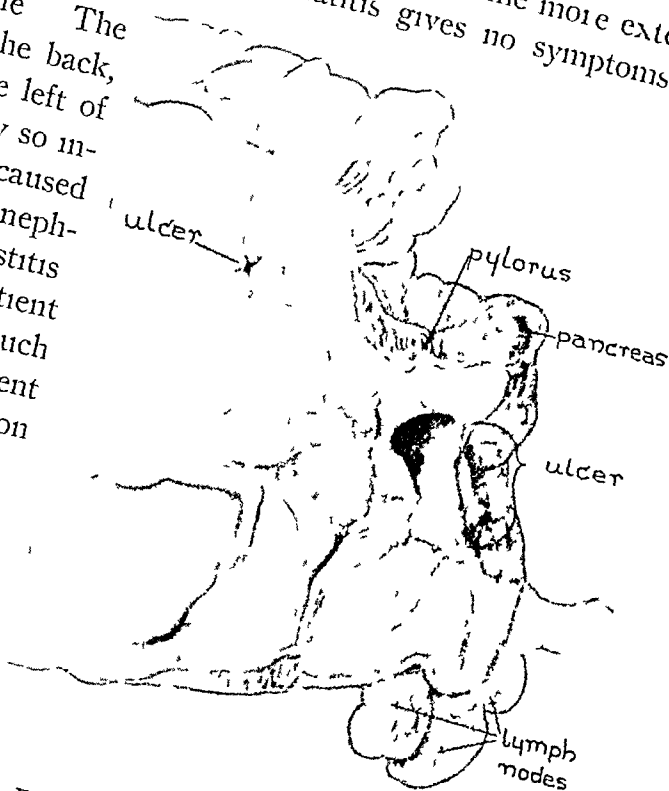
Relief by food, soda or vomiting is not constant and there is a sense of discomfort and a tenderness on pressure in the upper abdomen which was not present before the perforation. When the perforation actually occurs pain may be severe.

Medical treatment after the perforation is not so effective as before the perforation. There is also considerable danger of bleeding. The vascular tissues of the pancreas tend to bleed quite freely, particularly if the perforation is large, and the hemorrhage may be profuse. A posterior perforating ulcer of the pyloric sphincter gives added symptoms of discomfort and obstruction because of the spasm of the sphincter and local edema. Roentgenologic examination is not always convincing, especially if the ulcer is within the grasp of the pyloric sphincter.

* Read before the American Surgical Association, Hot Springs, Va. May 11, 12, 13

PEPTIC ULCERS

The pathologic picture also changes, because, in addition to the lesion in the stomach, there is some degree of pancreatitis. The pancreatitis is usually local around the region of the perforation but it may become more extensive. Unless it spreads, the associated local pancreatitis gives no symptoms of a disturbed function of this gland and laboratory tests are futile. The pain is often referred to the back, either to the right or to the left of the spine, and is occasionally so intense as to resemble the pain caused by a stone in the kidney, by nephralgia, or by acute cholecystitis. The previous history of the patient with peptic ulcer should aid much in the diagnosis of the subsequent events when there is perforation into the pancreas.



Case 1—As an illustrative case Mrs J H A, Path No 13684, white, age 48, was admitted to the hospital, July, 1938. The gallbladder containing a stone, had been removed elsewhere ten years previously. The patient, however, continued to suffer with indigestion. On admission the symptoms of pain and discomfort pointed to the back and to the right kidney, so a gastro-intestinal roentgenologic examination was not made, but a complete urologic study was made. The right kidney was enlarged and somewhat prolapsed. There was slight pain in the epigastric region, though this was not marked. The diagnosis of nephralgia seemed probable. On opening the abdomen for exploration a duodenal ulcer, which had perforated into the upper part of the head of the pancreas, with inflammatory involvement of the surrounding tissues, was found (Fig 2). A partial gastrectomy was performed and the patient recovered with complete relief of her symptoms. Under date of April 7, 1939, she reports, "I can eat almost anything without discomfort. Before the operation I was suffering intense pain all the time, but now I am free from pain and have gained 21 pounds."

Fig 1—Path No 8462 W G M, white male age 66. Specimen of stomach measured 10 cm on the lesser curvature and 17 cm on the greater curvature. Much of the gastric mucosa was congested. There was a gastric ulcer about 5.5 cm from the pylorus on the lesser curvature, and within the grasp of the pyloric sphincter was a deep oblong ulcer which had perforated into the pancreas. There were large lymph nodes on the lower border of the stomach. A Hofmeister operation was performed June 11, 1929, and a layer of pancreatic tissue was excised with the base of the ulcer. The patient is now entirely symptom free and says (April 4, 1939) that he has "had no pain since leaving the hospital ten years ago." There were only two Hofmeister operations in this series of cases.

* The anatomists are reluctant to commit themselves about the measurements and capacity of the stomach because it varies so much, but Jackson, in Morris's Human Anatomy, 9th edition states that the lesser curvature of the stomach averages about 10 cm (7.5 to 15 cm), and that the greater curvature is three or four times as long. In these specimens there is usually about 2 cm length along the curvatures appear larger.

Not infrequently, in cases of persistent pain or discomfort unrelieved by medical treatment when a peptic ulcer has been demonstrated in the anterior wall of the duodenum, there exists in the posterior wall another ulcer that has

perforated into the pancreas. One should not be deceived, then, by an ulcer in the anterior wall of the duodenum into thinking that it is the only lesion.

After sifting the cases that are not cured by medical treatment, Hinton reports on adherent posterior duodenal ulcers and states that for the past four years and nine months the operation he has performed for all duodenal ulcers has been a subtotal gastrectomy. He emphasizes the fact that the inflammatory lesion itself should be removed, and if this is done primarily the mortality rate is lowered. In 48 primary subtotal resections there were two deaths, a mortality rate of 4.1 per cent. In 16 secondary gastric operations there were five deaths, a mortality rate of 31 per cent. In the entire series of 64 cases there were seven deaths, with a mortality rate of 10.9 per cent.

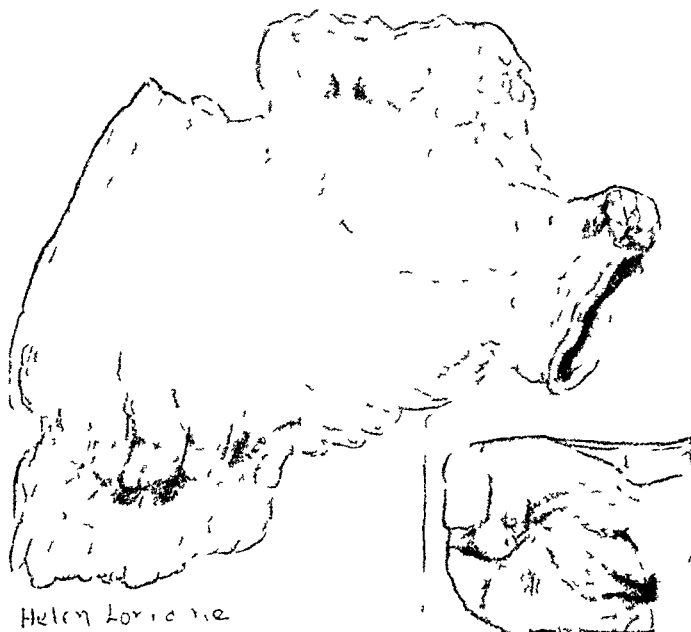


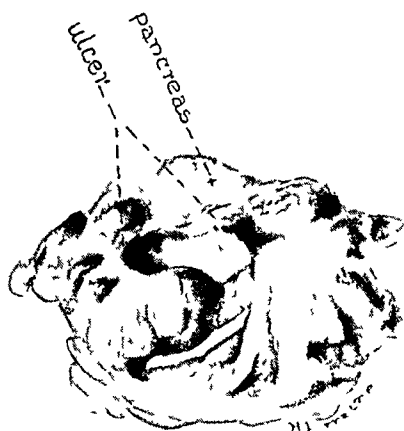
FIG 2—Path No 13684 J H A, white, female, age 48. Specimen of stomach measures 15 cm along the lesser curvature and 18 cm along the greater curvature. At the upper posterior part of the duodenum is a prolongation of the duodenum which is covered with pancreatic tissue removed. The insert shows the internal view of the ulcer which had penetrated into the pancreas.

CASE REPORTS

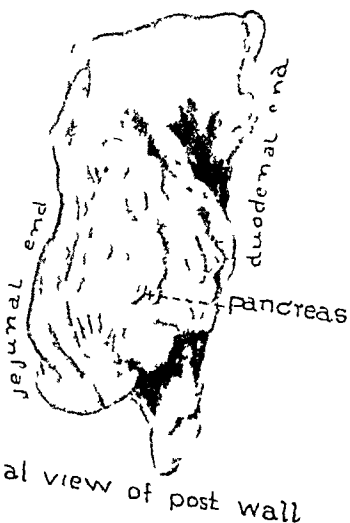
During a period of ten years, from December 31, 1928, to December 31, 1938, I have operated upon 20 cases of peptic ulcer of the stomach or duodenum that had perforated into the pancreas. In all of these cases a partial gastrectomy was performed in 18, by a modification of the Billroth I type described elsewhere, in which the upper border of the stomach is united to the upper border of the duodenum and the duodenum is flared open. In two cases this operation could not be applied, and a Hofmeister modification of the Billroth II type was performed.

Nine of the ulcers were duodenal, nine were gastric, one was a duodenal-jejunal ulcer, and in one case there were both a duodenal and a gastric ulcer. Five of the gastric ulcers were within the grasp of the pyloric sphincter.

PEPTIC ULCERS



View of ulcer through jejunal
end of specimen



External view of post wall

FIG 3—Path No 9247 L E white male age 46 Section of specimen showing the terminal duodenum and the first part of the jejunum together with the base of the ulcer which had perforated into the pancreas On the right there is a posterior view showing the pancreatic tissue that was removed along with the specimen



FIG 4—Path No 12755 D D, white, male, age 69 Operation February 17 1937 The specimen of the stomach measures 10.5 cm along the lesser curvature and 15 cm along the greater curvature In the upper posterior wall about 2 cm from the cardiac end of the specimen is an excavating ulcer 1.75 cm in diameter The specimen shows a layer of pancreatic tissue which has been removed with the ulcer The insert shows the interior view of the ulcer The patient reported April 3 1939 that he is completely cured I have not been sick a day since I left the hospital

The only death in this series of cases was of a patient in whom it was impossible to remove the ulcer. A Hofmeister operation was performed. A report of this case is as follows:

Case 2—Path No 11695 T B B, white, male, age 39, had a history of several massive hemorrhages from the stomach and the passage of tarry stools. One hemorrhage occurred March 5, 1935, and on March 22, there was another large hemorrhage. An analysis of the gastric juice showed the HCl 56, with total acids 78. The hemoglobin was 25 per cent, red blood cells 1,520,000, and white blood cell count 5,200. March 23, a partial gastrectomy was performed. In the posterior wall of the duodenum there was an ulcer, so large that it could not be removed. It began about two centimeters from the pylorus and penetrated into the head of the pancreas. It was not bleeding then, but the base was necrotic. It extended to a point near the ampulla of Vater. The upper sides of the ulcer were undermined with a cautery in order to close the duodenum, and a Hofmeister operation (Billroth II) was performed. The patient was given a transfusion of blood. He did well for eight days, when he had a sudden attack of intense pain and his blood pressure sank to 70 systolic. It was thought that there was a perforation. He was given another transfusion, and under local anesthesia the abdomen was opened. No evidence of peritonitis could be found. There was a large mass about the head of the pancreas. A jejunostomy was performed for feeding. The patient died the following day. Necropsy showed the general peritoneal cavity about normal, with no free fluid. The suture line involving the union of the stomach and jejunum and the enterostomy were in good condition. The lesser peritoneal cavity which had been walled-off by adhesions was filled with thin pus. The infection probably came from the large ulcer through the lymphatics. The ulcer involved much of the head of the pancreas. In the center of the ulcer was a large vein, the midportion of which had been destroyed. Both ends of the vein were occluded with a well organized thrombus. The quick development of the infection simulated a perforation into the peritoneal cavity.

There was one case of ulcer diathesis, in which there were recurrences after operations performed elsewhere and by me. Medical treatment afforded no relief.

Case 3—Path No 9247, L E, white, male, age 46, gave a history of having been operated upon elsewhere in 1922, a gastro-enterostomy was performed. One and one-half years later, there was an excision of a recurrent ulcer and separation of adhesions. Another operation for adhesions was performed, then a pyloroplasty, and finally another gastro-enterostomy was performed. He was admitted to St Elizabeth's Hospital in August, 1930. Analysis of the gastric juice showed HCl 55, with total acids of 67. In the terminal duodenum and the first part of the jejunum there was an extensive ulcer that had perforated into the pancreas. The gastro-enterostomy was disconnected, the segment of affected bowel was dissected from the pancreas with a cautery, resected, and an end-to-end union was made with much difficulty, a partial gastrectomy of the modified Billroth I type was then performed (Fig 3). Four days later, because of obstruction at the site of the intestinal resection, a jejunostomy was performed. After this, the patient made a fairly satisfactory recovery and the obstruction disappeared, but six months later he had symptoms of a recurrent ulcer. He was operated upon again. There was a large anterior perforated ulcer involving the stomach, duodenum and colon. The perforations were closed, but the patient gradually sank and died eight days later.

This case is not the usual type of case being considered, for it was a perforation of the terminal part of the duodenum along with the jejunum and it occurred after several previous operations performed elsewhere, but it is included because the duodenum was involved.

These cases of ulcei diathesis are, fortunately, rather rare, but they are extremely puzzling. It seems radical, but after all other means fail a total gastrectomy might be considered. The two cases that had recurrent symptoms after partial gastrectomy are appended.

Case 4—Path No 12130 R E C, white, male, age 47. The patient suffered intensely. The gastric juice showed HCl 18, total acids 38. January 10, 1935, a partial gastrectomy was performed for a posterior perforating ulcer, which was chiefly in the duodenum but extended into the grasp of the pyloric sphincter.⁵ There was much inflammation and infiltration around this ulcer. He made a fairly satisfactory recovery, but a few months later began having further symptoms, and in February, 1936, he was again operated upon. There was an extensive inflammatory exudate about the junction of the stomach and



FIG 5—Path No 13488 R E M, white, male, age 41. Partial gastrectomy April 9, 1938. The specimen of the stomach measured 11 cm along the lesser curvature and 17 cm along the greater curvature. The distal half showed evidence of gastritis with some punctate erosions. In the lower posterior portion of the duodenum there was a perforating ulcer measuring 1.25 x 0.75 cm which involved the pancreas.

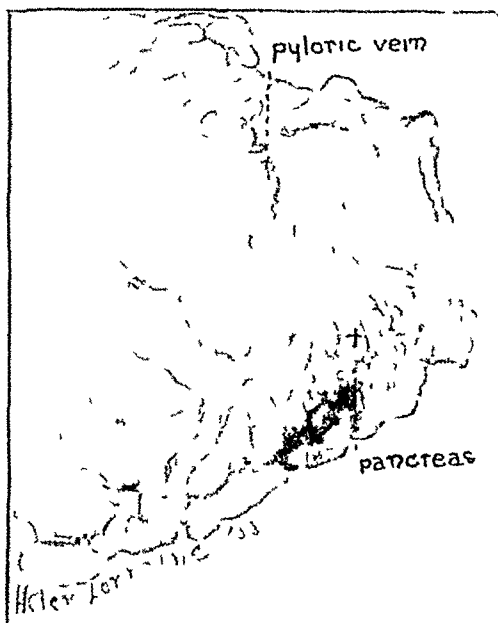


FIG 6—R E M. Posterior surface of the specimen shown in Figure 5, with the pancreatic tissue attached. In the lower portion, and just beneath the ulcer in the pancreas, were several large vessels from which the hemorrhage probably came.

duodenum. No effort was made to disturb these adhesions, but when the stomach was opened for a gastro-enterostomy the interior was explored with the finger. An ulcer, apparently about two centimeters in diameter, could be palpated on the lower and somewhat posterior portion of the stomach near the site of the previous resection. There was a wide opening between the stomach and duodenum. The ulcer did not appear to be malignant. A posterior gastro-enterostomy was performed, with a temporary jejunostomy for feeding. He made a satisfactory recovery. Under date of April 5, 1939, he reports "I am entirely free from any symptoms of stomach trouble whatsoever."

Case 5—Path No 13488 R E M, white, male, age 41, had had a perforated duodenal ulcer from which there had been two massive hemorrhages and which did not respond to medical treatment. There had been symptoms for two or three years. The patient was high-strung and nervous. The gastric juice showed HCl 70, and total acids 98. A partial gastrectomy with removal of the adherent part of the pancreas was per-

formed April 9, 1938. The ulcer was in the lower, posterior portion of the duodenum and measured 1.25 x 0.75 cm. There was gastritis with a few punctate erosions in the pyloric portion of the stomach (Figs 5 and 6). The patient made a satisfactory recovery and was well for a while, but the discomfort recurred, though there was no further hemorrhage and the symptoms were not so severe as before the operation. He was again operated upon November 10, 1938. There was extensive reaction about the site of the anastomosis of the stomach and duodenum. The stomach was drawn up high and was rather small. A posterior gastro-enterostomy was performed. Exploration of the pyloric end of the stomach could not be made, but from the surrounding inflammation and exudate, it seems probable that he had a recurrent ulcer. He reported in April, 1939, that he is now symptom-free.

In these two cases of failure to permanently relieve the clinical symptoms, apparent cure has been obtained by a secondary operation of gastro-enterostomy. Both of these patients were nervous and high-strung men, a type apt to have a recurrence of ulcer after any gastric operation. It would seem better to have performed a primary partial gastrectomy, by which the patient was temporarily relieved, and a gastro-enterostomy later, than to have performed

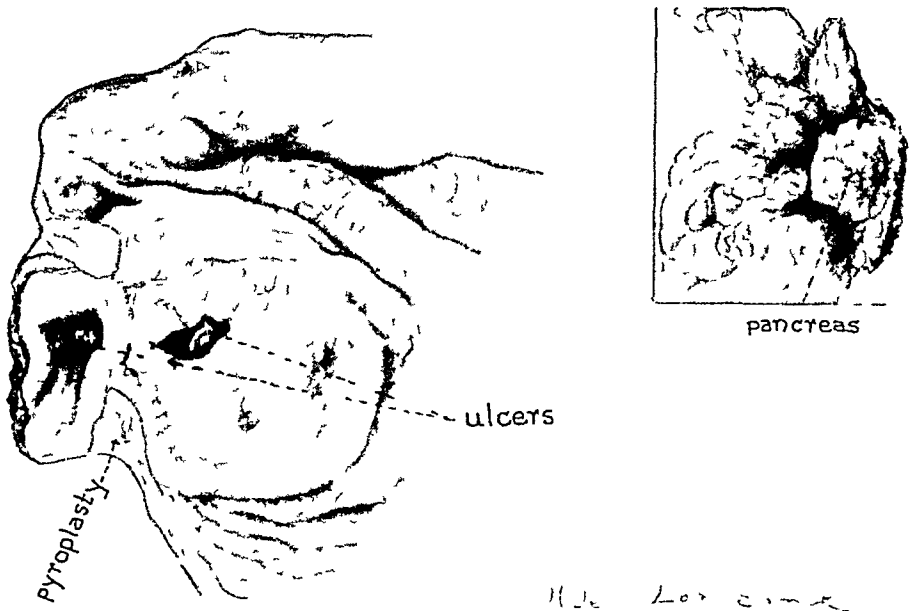


FIG 7—Path No 12831. A V H white male age 52. Operation April 27 1937. Specimen of the stomach measured 16 cm along the lesser curvature and 25 cm along the greater curvature. On the posterior surface of the stomach near the pyloric sphincter was some adherent pancreatic tissue which was dissected off with the crutery. The stomach showed evidence of gastritis and there was a pouch, probably resulting from a preceding pyloroplasty. There were two peptic ulcers—one in the stomach and one in the duodenum.

a primary gastro-enterostomy, with the probability in these two cases of a secondary jejunal ulcer which would involve the more difficult subsequent procedure of taking down the gastro-enterostomy and resecting the stomach.

There are two patients who may be classed as improved but not cured by the partial gastrectomy.

Case 6—Path No 12831. A V H white male, age 52, was operated upon June 30, 1928. A gastro-enterostomy, which had been performed elsewhere six years previously, was disconnected, and a pyloroplasty was performed. The patient did fairly well

for seven years, then he had a lesion about the pyloric portion of the stomach. The gastric juice showed HCl 37, total acids 57. A partial gastrectomy was performed, April 27, 1937. There were two peptic ulcers, one in the stomach and one in the duodenum. Both had perforated into the pancreas, and in both there was a base of pancreatic tissue attached to the specimen (Fig 7). He reports now that he is better, though he still has some gastric symptoms, but is "taking life easy" and is fairly comfortable.

Case 7—Path No 13512 V C T, white, male, age 51, had a large ulcer of the pyloric portion of the stomach penetrating into the pancreas. The gastric juice showed HCl 50, and total acids 60. He made a satisfactory recovery from a partial gastrectomy performed April 22, 1938, but at present states he has gastric symptoms, unless he ad-



FIG 8—Path No 13993 D N S white male age 50. Partial gastrectomy December 19, 1938. Specimen of the stomach measured 6 cm along the lesser curvature and 16 cm along the greater curvature. On section there was a deeply perforating ulcer in the upper posterior part of the pyloric sphincter, more on the stomach side than on the duodenal. It measured 0.5 x 1 cm. Attached posteriorly, was a segment of pancreatic tissue into which the ulcer had perforated. The patient reported April 3, 1939, that he was free from symptoms and "feeling better than I have felt for a long time."

heres closely to an ulcer diet. He may be classed as improved. In his history, taken before the operation, the following significant paragraph appears: "He has always been a gluttonous type of eater, and tells of eating as many as 10 or 12 biscuits at a meal, of drinking rather heavily at times in the past, and other such severe insults to his gastrointestinal tract."

An ulcer of the stomach perforating into the pancreas may resemble a peptic ulcer clinically and even in gross appearance and yet be malignant.

Case 8—Path No 10792 C G W, white, male, age 31, had high acid values in the gastric juice (HCl 74 and total acids 86), and marked gastric symptoms. A partial gastrectomy showed two ulcers in the pyloric portion of the stomach, one had perforated into the pancreas. Grossly, they resembled very closely peptic ulcers, but microscopically, they proved to be small cell carcinoma. There was a recurrence of extensive carcinoma and death within nine months.

In addition to the cases herewith reported, in which a peptic ulcer perforating into the pancreas was demonstrated in the specimen removed, there were three patients with what appeared to be a duodenal ulcer perforating into the pancreas upon whom a posterior gastro-enterostomy was performed after loosely tying off the pyloric end of the stomach. These patients recovered satisfactorily. There were dense adhesions with an extensive exudate into the surrounding tissues, and the duodenum was fixed to the pancreas. However, this marked inflammatory reaction may have been from an accompanying duodenitis. The tissues were so welded together by firm lymphatic exudate that partial gastrectomy would have been unduly dangerous. As these lesions could not be demonstrated to be posterior perforating ulcers, they are not included in this list.



FIG 9.—D N S Posterior surface of specimen shown in Figure 8 with the pancreatic tissue attached

The intense reaction in such instances would seem, too, to indicate a high resistance and a probability of recovery if some help is afforded by diversion of the gastric contents and by giving the tissues rest by ligating the pyloric end of the stomach just tightly enough to occlude without strangulation. Doubtless, the chronic cases, in which the lesion remains, have not sufficient resistance for healing, and it becomes necessary to remove the lesion (Table I).

Treatment—The technic used in all but two of these cases is essentially the same as that previously described in several publications. It is a modification of the Billroth I type of operation in which the lesser curvature of the stomach is aligned to the upper border of the duodenum, and the duodenum is flared open to prevent obstruction. However, the procedure has to be altered somewhat in individual cases. After dividing and tying the segments of the gastrocolic omentum from the point of the proposed resection to the pylorus, and the vessels along the lesser curvature in the gastrohepatic omentum, the portion of the stomach to be removed remains attached only by its two ends and by the adherent ulcer. Two Payr clamps are placed on the body of the stomach, which is divided between them with an electric cautery. Usually the lesion will prevent the placing of a clamp on the duodenum. The stomach is then lifted up, and, with a very hot electric cautery, the adherent pancreas is shaved off as a thin slice, care being taken not to open the ulcer. This can best be done by approaching the adherent region carefully and freeing it to some extent on each side. Too much of the pancreas should not be removed (Fig 10). If the ulcer is accidentally opened the opening is plugged with

SYNOPSIS OF 20 CASES OF PARTIAL GASTRECTOMY FOR PEPTIC ULCER PRIOR TO THE PANCREAS

TABLE I

December 31, 1928, through December 31, 1938

No	Date	Sex		Location	Previous Operations for Ulcer	Operation		Subsequent Gastro-enterostomy	Result		
		M	F			Mod Bil I	Hof		Well	Imp	Re-curred
1	6-11-29	M		Duodenum	(1) Gastro-enterostomy						
2	8-8-30	M		Duo-jej	(2) Exc rec ulcer						
3	10-30-30		F	Duodenum	(3) Pyloroplasty						
4	10-21-31		F	Duodenum	(4) Gastro-enterostomy						
5	9-16-33	M		Stomach							
6	8-11-34	M		Stomach							
7	11-7-34		F	Duodenum	Sut perf ulcer 1 yr before, elsewhere						
8	1-10-35	M		Stomach							
9	3-23-35	M		Duodenum							
10	10-12-36	M		Duodenum							
11	2-17-37	M		Stomach							
12	4-2-37	M		Stomach							
13	4-27-37	M		Duodenum							
14	5-17-37	M		and stomach	(1) Gastro-enterostomy						
15	4-9-38	M		Duodenum	(2) Pyloroplasty						
16	4-22-38	M		Duodenum							
17	7-15-38		F	Stomach							
18	8-15-38	M		Duodenum							
19	10-21-38	M		Duodenum							
20	12-19-38	M		Stomach							
Totals		16	4			18	2	2	16	2	1

wet gauze or the finger is inserted into it. Then, with tension on the stomach, the rest of the adherent stump of pancreas is cut off. If the cautery is quite hot and the stomach is lifted up, a thin slice of the pancreas can be quickly removed without burning one's finger. If the ulcer is in the stomach, after freeing it, the duodenum is separated from the pancreas and cut across with the cautery, catching the margins of the duodenum as the incision is made. The duodenal contents are removed with a suction apparatus and a sponge moistened with salt solution is gently placed in the duodenum. If the perforation is from a duodenal ulcer, the base of the ulcer is shaved off in a similar way. The operation here is somewhat more difficult because of the shortness of the stump of the duodenum, but this technic can be carried out,

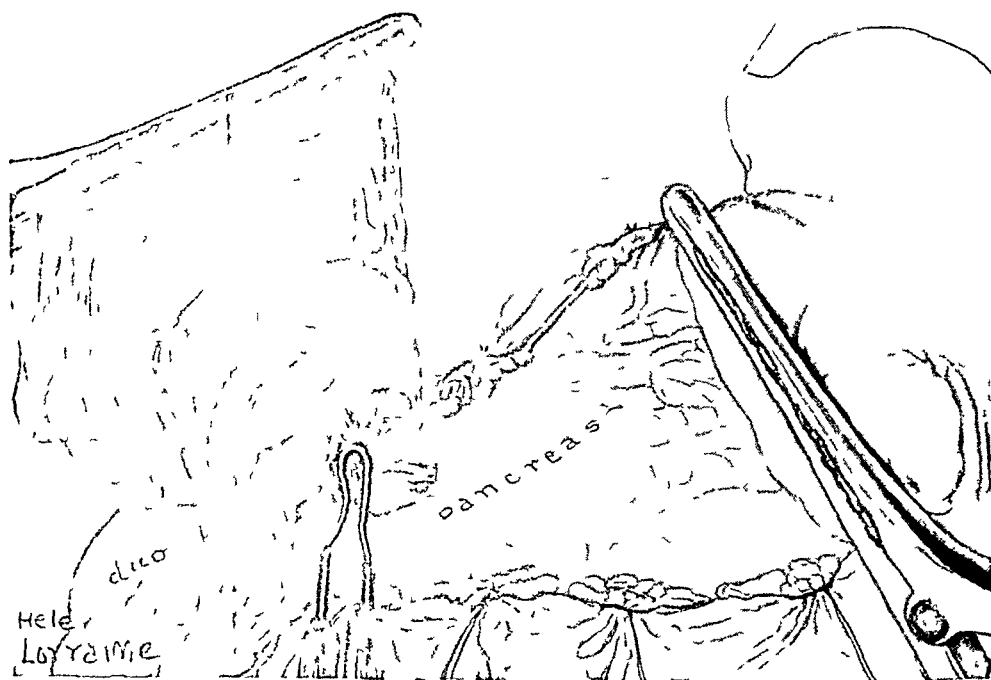


FIG. 10.—The stomach has been divided between two Payr clamps and the distal end is lifted up while the slice of pancreatic tissue which forms the base of a penetrating ulcer is being shaved off with the hot electric cautery.

probably more satisfactorily, in these cases than the Billroth II type of partial gastrectomy if the ulcer is removed because with a very short stump of the duodenum resulting from the excision of the ulcerated area it becomes difficult to close the stump of the duodenum effectively. If there is back pressure which occurs not infrequently after the Billroth II operation, a duodenal fistula may result, whereas in this type of operation the posterior wall of the stump of the stomach is tucked in by the short posterior wall of the stump of the duodenum and sutured. This makes the situation in this region comparatively safe because the wound in the pancreas has been made with the cautery and is sterile and the peritoneum on the posterior surface of the stomach will readily unite to the short posterior stump of the duodenum and the denuded pancreas. Then too this sutured area is over the solid surface of the pan-

creas, and if there is not an accurate healing at this point the charred and sterile pancreatic wound will act as a bumper of safety

A Stab Wound Gastrostomy—To give the stomach postoperative rest it is essential that the contents of the stomach be removed and dilatation prevented, which is usually accomplished by the insertion of a Jutte or Levine tube into the stomach through the nose. In some patients the presence of the tube is quite a nuisance. If it stays in constantly for a few days it often irritates the



FIG 11—The first stage of a tube gastrostomy. After uniting the posterior margin of the stump of the stomach to the posterior margin of the stump of the duodenum, a sharp hemostat is thrust through the anterior wall of the stomach near the greater curvature. It grasps the end of a soft rubber catheter in which there is an additional perforation, and draws it into the stomach. The catheter may be introduced through a stab wound to the left of the incision before this is done, or it may be clamped at its middle and after being drawn into the stomach the butt end can be carried through a stab wound in the abdominal wall after the stomach and duodenum have been sutured together.

(A) After drawing about three inches of the catheter into the stomach the catheter is fastened to the stomach with a single suture of fine chromic catgut, and a purse string suture is placed around the catheter.

(B) The stomach is being pulled snugly to the anterior parietal peritoneum. A few sutures of fine chromic catgut are placed, after which a tag of omental fat is fastened around the tube.

nose and throat, and if it has to be inserted every few hours, the repeated insertions are even more disagreeable than having the tube remain. Recently I have employed a gastrostomy, which is much more comfortable to the patient and more efficient for drainage than the nasal tube. This is done as follows:

After the posterior row of sutures uniting the stomach to the duodenum is placed, a sharp-pointed hemostat is thrust (directly, not obliquely) through the stomach from within outward at a point on its anterior wall near the greater curvature, where the stomach can be easily brought into contact with

the abdominal wall. A soft rubber catheter, No. 18, in which an additional perforation has been made near the end, and which is clamped at its middle, is caught with the hemostat and drawn into the stomach (Fig. 11). After three or four inches of the catheter are within the stomach, the catheter is fastened to the gastric wall by a suture of fine chromic catgut and a purse-string suture of chromic catgut is placed around it. The butt of the catheter is drawn through a stab wound in the abdominal wall, and then clamped, and the clamp on its middle is removed. The catheter is gently pulled upon until the stomach is in contact with the parietal peritoneum. Sutures of fine chromic catgut are placed between the stomach and the parietal peritoneum and some omental fat is brought around this point of contact (Fig. 11B). The fat not only adds to the security of the punctured wound, but may prevent a subsequent tight adhesion.

By this method the muscular layers of the stomach are not cut, as would occur if a knife were used to make the puncture, then fibers are merely pushed apart as are the muscular bundles of the abdomen in making a McBurney incision. The catheter fits in snugly, and there is usually no leakage after the catheter has been removed.

CONCLUSIONS

There seems to be some danger of rather extensive pancreatitis from an ulcer that has perforated into the pancreas. With the base of the ulcer consisting of pancreatic tissue, if the operation is delayed too long it may well be that the residual pancreatitis will not clear up promptly.

The advantages of this procedure are that the ulcer is removed along with the superficially infected portion of the pancreas, the stomach empties physiologically into the duodenum, which is more resistant to the gastric juice than the jejunum, the region of trauma is limited to one field, and if there is a recurrent ulcer a posterior gastro-enterostomy can readily be performed. A primary gastro-enterostomy, which leaves this lesion *in situ*, does not appear to be logical, though there may be circumstances in which it is the only operation indicated, as when the reaction around the ulcer is extensive.

The mortality rate should not be great. In these patients, in which this type of operation has been performed, there has been no operative death. The only death following operation was in a patient in whom this procedure was not possible because of the extent of the ulcer. The ulcer could not be excised, and the Hofmeister-Billroth II type of operation had to be performed.

A simple method of making a gastrostomy to substitute for using the nasal tube is described.

REFERENCES

- ¹ Church, R. E., and Hinton, J. W. A Study of 671 Cases of Peptic Ulcer with Special Emphasis on 114 Postoperative Cases. *New York State Jour. Med.*, 34, 1079, December 15, 1934.
- ² Hinton, J. W. Adherent Posterior Duodenal Ulcer. *Arch. Surg.*, 37, 944-948, December, 1938.

- * Horsley, J. Shelton. *Surgery of the Stomach and Duodenum*. C. V. Mosby Co., St. Louis, 1933.
- ¹ Horsley, J. Shelton. *The Surgical Treatment of Cancer of the Stomach*. *Surg., Gynec., and Obstet.*, 60, 486-494, February 15, 1935.
- ² Horsley, J. Shelton. *Ulcer of the Pyloric Sphincter*. *ANNALS OF SURGERY*, 103, 738-746, May, 1936.
- ³ Horsley, J. Shelton, and Bigger, I. A. *Operative Surgery*. 4th ed., C. V. Mosby Co., St. Louis, 1937.
- ⁷ Lewisohn, R. *Gastrojejunal and Jejunal Ulcer*. *J. A. M. A.*, 77, 442-448, 1921.
- ⁸ Lewisohn, R. *The Frequency of Gastrojejunal Ulcers*. *Surg., Gynec., and Obstet.*, 40, 70-76, 1925.

DISCUSSION—DR. JOHN M. T. FINNEY, JR. (Baltimore, Md.) I feel that there are two points in stomach surgery which Doctor Horsley's procedure calls to our attention immediately. The first is the now pretty well recognized principle of the necessity of resection of the stomach in these cases of ulcer perforating into the head of the pancreas, the necessity resting principally on the control of hemorrhage.

It has been shown by a great many people that because of the location of the main vessels in the blood supply to the pylorus and the upper duodenum, these ulcers perforating into the head of the pancreas are prone to hemorrhage, and hemorrhage of severe proportions, and that it is almost impossible to obliterate these vessels, to properly tie them and control the hemorrhage thereby, unless one resects the stomach.

Of course the resection of the stomach accomplishes another thing, also, and that is, providing the resection is extensive enough, the removal of a sufficient quantity of the acid bearing area of the stomach to materially reduce the free acid after the operation and thereby control, at least to a certain extent, the recurrence of marginal ulcers following the resection.

The second principle is, I think, probably much more debatable than the first. What type of anastomosis one is going to perform following the resection. We feel, as does Doctor Horsley, that, where it is possible to maintain the normal anatomicophysiologic basis, anastomosis of stomach to duodenum, it is much more preferable than the anastomosis of stump of stomach to jejunum. This is not always possible, but where it is possible, I feel, as I am sure Doctor Horsley does, that one can reduce materially the incidence of postoperative marginal ulceration.

I do not altogether agree with Doctor Horsley on the method of this anastomosis. Personally, I much prefer an end-to-side anastomosis into the stump of the duodenum, having closed the stump, than the end-to-end of the Billroth I procedure. I think it is preferable because it does not have the tendency to constriction at the site of anastomosis, and one is not limited by the diameter of the stump of the duodenum in the size of that anastomosis.

By having a larger anastomosis, one accomplishes two things. First, it removes the possibility of future obstruction or interference with proper emptying of the stomach, and secondly, by getting quite a wide anastomotic opening, one insures the rapid neutralization of such gastric acidity as is left by immediate mixing with the alkaline duodenal contents. This we feel can be better accomplished by putting the cut end of the stomach into the side of the duodenum where one is not limited in any way by the diameter of the duodenum.

As for the type of gastrostomy which Doctor Horsley has described, I have had no experience whatever. It does seem that it possibly offers a very useful adjunct at times when one has a patient where it is reasonable to suppose he or she will not tolerate the use of a nasal tube postoperatively.

DR FRANK H LAHEY (Boston) While this ulcer problem has been quite well threshed over, we all ought to relate our experiences with it because it is still an unsettled one. It is very evident that operative procedures for ulcer are by no means standardized. First of all, I do not think that 80 per cent of these patients get well with medical treatment.

I dislike to speak of figures, but they must be mentioned. We have now had 3,500 patients with ulcers in bed under bad management. Only 8 per cent of the patients with duodenal ulcer have been operated upon, and only 23 per cent of those with gastric ulcer, but all the others are not well. On the other hand, they are not sufficiently ill so that they need to have an operation and subtotal gastrectomy.

As to the problem of surgical management, I disagree definitely with any procedure which may incline one to make anything but radical removals of large portions of the stomach in patients who have had repeated hemorrhages or who possess the other features of failure under medical measures. Any procedure, such as the Billroth I operation, that attempts to attach a short stump of the stomach to the fixed duodenum will very definitely incline one to make inadequate gastric resections. We are, therefore, not interested in any type of procedure of dumping gastric contents into the duodenum at the expense of radical removal of large parts of the stomach.

There are one or two other points, based upon our experience representing now something over 200 subtotal gastrectomies for ulcer. An important point, I think, in the management of duodenal ulcers is first to settle the relation of the ulcer to the common bile duct. I know nothing that has been more distressing to me than to resect the portion of the duodenum containing the ulcer and then find I did not have enough duodenum left to satisfactorily and safely close it.

The other point that I wish to make is that we now have performed the Finsterer resection by exclusion operation in 20 cases. This consists of leaving the ulcer when it is not one in which recent hemorrhage has occurred, turning the end of the stomach in proximal to the pylorus, then performing a high gastric resection. The end-results of these followed cases have been just as satisfactory as have been the cases in which subtotal gastrectomy together with removal of the ulcer-bearing duodenum has been performed.

One other fact is that when you attempt to perform subtotal gastrectomy with clamps, you will be limited in the height of the resection. When you undertake them without clamps, you can resect them as high as you want to.

DR ROSCOE R GRAHAM (Toronto, Canada) I should like to ask Doctor Horsley if he has had any pancreatic fistulae follow in these cases. We have had experiences that are at variance with his. In a group of cases, when a portion of pancreatic tissue was resected together with the ulcer, the convalescence was complicated too often by a pancreatitis, which in one instance proved fatal. In a second group of cases, when we have interfered with the pancreas when a penetrating posterior wall duodenal ulcer was present, and then restored the continuity of the gastro-intestinal tract by an end-to-end anastomosis of stomach to duodenum, we had, in two such cases, within three months, a recurrence of ulcer at the line of anastomosis. We, therefore, now never establish continuity of the gastro-intestinal tract following an operation for duodenal ulcer unless we have been able to remove all evidence of local pathology. In view of the fact that we believe surgical procedures, and particularly gastrectomy, are contraindicated except in complicated duodenal ulcers, it becomes obvious that it is rarely possible to carry out this procedure.

With adequate preoperative preparation by means of an indwelling duodenal tube over a period ranging from two to three weeks, we believe that the

risk of opening the proximal gastro-intestinal tract is not great. This is based upon the fact that repeated lavage decreases the associated periduodenal edema which involves not only the pancreas, but other periduodenal tissues. With this belief, we pinch off the duodenum from the ulcer base, which is left *in situ* on the pancreas, and is exteriorized by closing the duodenum and then turning the closed end into the ulcer base, where it is held by interrupted silk sutures. This, in our hands, has obviated the postoperative complications of pancreatitis.

I should like again to emphasize the point which Doctor Lahey has made, that there very rarely is any indication for an operation for duodenal ulcer which is combined with restoration of the gastro-intestinal tract in continuity, not for the reason which he stated, that it is impossible to perform a sufficiently adequate resection, as we believe this is possible, and we practice it in the gastric ulcers, but because in our experience the incidence of recurring ulcer at the site of the anastomosis is high. We are convinced in such cases that a radical subtotal gastrectomy, with removal of the entire lesser curvature, which is readily accomplished with the use of a Schoemaker clamp, offers the greatest safeguard for the patient's future.

DR J. SHELTON HORSLEY (closing). Some of the objections made have been dealt with in the paper. It was too long to read all of it.

In regard to Doctor Finney's preference for the end-to-end method, I will say that in perforating duodenal ulcers it is necessary to close the stump if an end-to-side of the stomach to the duodenum is done. If there is a duodenal perforating ulcer shaved from the pancreas, the stump of the duodenum is very short and the closure of the stump of the duodenum to make an end-to-side union is somewhat of a problem. If the duodenum is flared open by an incision as shown in the illustration, there is very little danger of constriction and the duodenum can be sutured to the stomach after bringing the posterior wall of the stomach, covered with peritoneum, over to the short stump of the duodenum and tucking it in. If the suture does happen to leak, there is a posterior solid wall of pancreatic tissue, made sterile by the cautery.

If there is a recurrent ulcer—in two of these cases I have had to do this—a posterior gastro-enterostomy is a much simpler procedure than performing a posterior gastro-enterostomy first, having a recurrent ulcer, and then disconnecting it and performing a partial gastrectomy.

As to the union of the stump of the stomach to the jejunum, in many of these cases there is a tendency to recurrence, and the farther down in the intestinal tract, the more sensitive is the mucosa to the acid of the stomach. Particularly in the type of case that suffers a great deal of discomfort, it seems to be much better to do what might be called a physiologic method by uniting the stump of the stomach to the stump of the duodenum along the lesser curvature and if there is a recurrence, it can be treated more simply later on by gastro-enterostomy.

As to the question of Doctor Graham, I have never had a pancreatic fistula in any of these cases. Remember that this is shaving off a very thin slice of adherent pancreas with the hot cautery. As to leaving the ulcer and performing a partial gastrectomy by the Finsterer method, of course many of these patients get well, but, after all, in the long run it seems better to follow physiologic lines and remove the infected ulcer than to leave it and unite the stomach to the jejunum.

If you leave a focus of infection, which the perforating ulcer is, you also leave a pancreatitis, which may extend and later the patient may be affected by this septic focus that you purposely left behind.

LATERAL GASTRODUODENOSTOMY IN CERTAIN CASES OF DUODENAL AND RECURRING ULCER*

VERNE C HUNT, M D

LOS ANGELES, CALIF

GRAHAM, among others, has directed attention to the many factors which require due consideration in the selection of the surgical procedure for ulcer which may be best suited in the individual instance. He said "The patient who accepts operation expects recovery from the operation, relief from the symptoms, security against recurrence, and restored economic efficiency. In order to achieve this desired result, the surgeon in determining the correct operative procedure must take into consideration the site of the ulcer, the character of the lesion, the associated physiologic disturbances, the result of the biochemical disturbances, and the age of the patient."

The variety of operative procedures which may be instituted in the surgical treatment of ulcer provides opportunity to achieve the desired result in a high percentage of instances, but for these results to be achieved requires versatility on the part of the surgeon. While a particular procedure may be executed upon many patients with ulcer, in whom the various factors approximate similarity, dissimilarity occurs so frequently that one must be prepared to select and execute that operation which most nearly accomplishes the purpose of surgical treatment in the particular instance.

It is not my intention at this time to discuss the relative merits of the various operations for duodenal and recurrent postoperative ulcers, suffice it to reiterate that no single operation is applicable in all instances of either type of ulcer. Broadly considered, the medical and surgical treatment of ulcer is directed toward control of gastric acidity and gastric secretion. Surgically, this may be accomplished either through neutralization and dilution by conservative operations, or through quantitative reduction of gastric acidity by partial gastrectomy. Even from a conservative viewpoint, a radical, partial gastrectomy may be and often is the operation of choice in certain cases of duodenal ulcer, particularly in those from which one or more massive hemorrhages have occurred, and in many cases of postoperative recurrent ulcer. Also, from a less conservative viewpoint, the magnitude of a partial gastrectomy may be, and not infrequently is, too great under certain circumstances when an opportunity is provided for the selection of a less drastic surgical procedure which may still accomplish the purpose of an operation with a minimum risk. The object of this discussion is to again direct attention to the merits of an operation which seems to justify its employment more often than it has been employed in the past.

The operation of lateral gastroduodenostomy is not new in principle, but

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

certain important details of recent contribution and materially in the execution of the operation and enhance the immediate and late result. In 1892 Jaboulay suggested, and, in 1894 first performed a gastroduodenostomy as an anastomosis between the upper portion of the second or descending portion of the duodenum with the anterior wall of the stomach. The duodenum was not mobilized, but the stomach was drawn over and sutured to it. Experiences with the operation of gastroduodenostomy have been reported by Kocher, Moynihan, Balfour, Wilkie, Reinhoff, Clute and others. J. M. T. Finney, Sr., was perhaps the first to mobilize the entire first part and upper half of the second portion of the duodenum. It is of interest that as he, the originator of the Finney pyloroplasty, and J. M. T. Finney, Jr., have had an increasing experience with the operation of pyloroplasty they have extended the incisions in both the stomach and the duodenum, thus providing a large stoma between the stomach and duodenum. In so doing, they have made duodenal content of a maximal degree of alkalinity available for neutralization or dilution of gastric content, at a level from which reflux of duodenal content into the stomach can readily occur. In other words, the operation of pyloroplasty has been extended to embrace the advantages of lateral gastroduodenostomy. Because the scope of the operation has been enlarged to include more of the stomach and the duodenum than the original procedure, it may hardly be considered a true pyloroplasty, and is best designated by the recently applied term, gastropyloroduodenostomy.

Physiologic Principles—Many observers agree that the reduction of gastric acidity, when it occurs following the conservative operations for duodenal ulcer, is due chiefly to an admixture of duodenal content with that of the stomach, and that perhaps most of the reduction of gastric acidity occurs through dilution instead of neutralization. In my own experience, the various types of pyloroplasty or operations confined to the pylorus, first portion of the duodenum and the prepyloric portion of the stomach, have been followed by results incomparable to those following practically all other types of operation instituted in the treatment of duodenal ulcer, and as a consequence have been abandoned. Most of the unsatisfactory results which follow operations upon the pylorus embracing division of or excision of a major portion of the pyloric muscle, with or without excision of the duodenal ulcer, have been due either to reactivation of a persisting ulcer in the posterior wall of the duodenum or to recurrence of an ulcer in the suture line of the pyloroplasty. In retrospect, this is as might be expected. The alkalinity of the duodenal content in the suprapapillary and in the subpapillary portions of the duodenum is not equal nor of the same degree. There is also considerable evidence which tends to support the idea that the reaction of the duodenal content in the first portion of the duodenum, particularly in patients who harbor an ulcer, is on the acid side rather than on the alkaline side. Furthermore that actual regurgitation of duodenal contents through a permanently abolished pyloric muscle in amounts sufficient to provide much diluent or neutralizing

effect, or that regurgitation occurs at all, have not been firmly established. The sum total of gastro-intestinal motility is downward and not upward. Considerable evidence is at hand to indicate that marked reduction in gastric acidity results when an admixture of duodenal and gastric contents occurs through a downstream by-pass and that little if any reduction results when such an admixture is dependent upon upstream regurgitation. Hill, Henrich and Wilhelmj, in a study of the changes in the gastric acidity in the experimental animal produced by various operations on the stomach, stated that after a Heineke-Mikulicz type of pyloroplasty the acid curve is almost the same as that in a normal dog, that after gastrojejunostomy the reduction in acidity is striking, and that after gastroduodenostomy the reduction is even more marked. Fundamentally, it would seem that the various operations designated as pyloroplasty fail to embrace the important principle in the surgical treatment of duodenal ulcer, namely, the control of gastric acidity and gastric secretion either through dilution and neutralization or through quantitative reduction.

Posterior gastro-enterostomy has been, and still remains, an operation of choice in many cases of duodenal ulcer, and when accurately executed in carefully selected cases it is followed by excellent results. Only one disconcerting factor—marginal or jejunal ulcer of variable incidence—limits its general usefulness. It is well known that the intestinal mucosa possesses or lacks (depending upon the segment) resistance to ulceration, and that perhaps the maximum degree of resistance exists in the second and third anatomic portions of the duodenum. Whether or not this is due to true inherent resistance in the mucosa or whether it is the result of the protection afforded the mucosa in these sections by the alkaline bile and pancreatic secretions remains a question. Without here presenting the evidence, the latter seems more probable. At any rate, it is now recognized that the degree of alkalinity of the duodenum is highest at the level and immediately below the papilla of Vater, as the result of the outpouring into the duodenum of bile and pancreatic secretion. While marginal, gastrojejunal or jejunal ulcer occurs with a variable frequency following posterior gastro-enterostomy, ulceration in or about the stoma of a lateral gastroduodenostomy seldom if ever occurs. Finney has said that an anastomotic ulcer does not follow, Flint, in his wide experience with the operation, has not seen an ulcer in the stoma of a gastroduodenostomy, Wilkie had two cases of stomal ulcer in his experience. In view of the physiologic processes concerned, lateral gastroduodenostomy should provide greater assurance against the development of an anastomotic ulcer than any other type of gastro-intestinal anastomosis excepting the Haberer end-to-side gastroduodenal anastomosis. It seems most probable that the greatest degree of dilution and neutralization of gastric acidity by duodenal contents is possible through a stoma at or just below the duodenal source of the diluent and neutralizing agents, bile and pancreatic secretions. Furthermore, it seems entirely logical that the mixing of duodenal contents of a maximum degree of alkalinity with gastric secretions at this level provides dilution and neutral-

zation at the proper time and place to be most effective. The experimental work of Graves and that of McCann suggests at least that the effectiveness of duodenal alkaline secretion upon gastric acidity is greater when it is emptied into the stomach downstream or into the prepyloric area than when it is diverted upstream into the fundus of the stomach.

Applicability of Lateral Gastroduodenostomy—Certain limitations in the applicability of lateral gastroduodenostomy exist and for the most part these are dependent upon anatomic relations and the mobilization of the duodenum. There are no true anatomic barriers to free mobilization of the third and

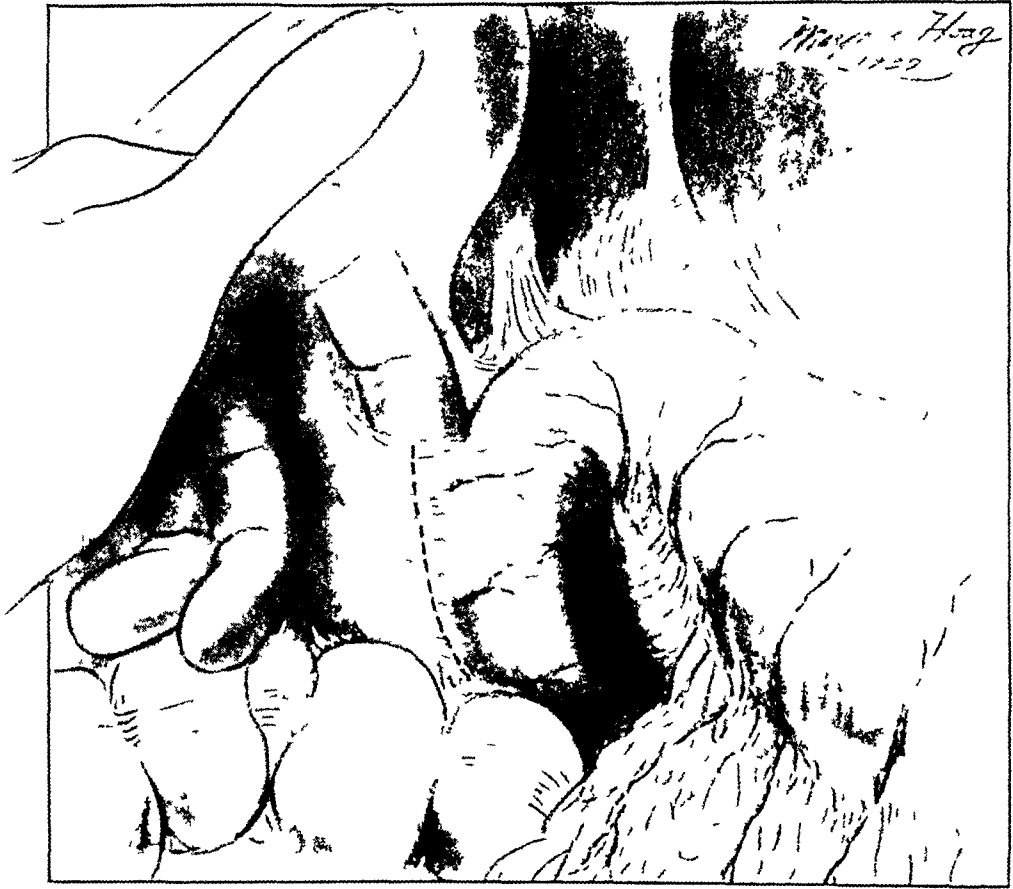


FIG. 1.—The filmy reflection of the peritoneum is divided lateral to the duodenum which allows elevation of the duodenum from its retroperitoneal position.

fourth portions of the duodenum except the superior mesenteric artery and vein which can be accurately visualized and preserved. In 1932, Reinhold described an infrapapillary gastroduodenostomy and stated that he had successfully operated upon 13 cases of chronic peptic ulcer by this method, with excellent results. His procedure facilitates anastomosis of the third portion of the duodenum with the antrum of the stomach through mobilization of the entire duodenum, including its fourth portion to and beyond the ligament of Treitz. In my own experience, such extensive mobilization has not been necessary. The filmy reflection of peritoneum overlying the duodenum is readily divided, thus facilitating the elevation of the duodenum from its retroperitoneal position for a liberal anastomosis without angulation (Fig. 1).

Clute and Sprague have recently illustrated methods by which angulation may be avoided

During the past few years lateral gastroduodenostomy has been employed in 22 cases, with no deaths and but few instances of temporary gastric retention, and has been followed by excellent results. In 13 cases, the operation was readily applicable as a primary operation of choice for duodenal ulcer in which either posterior gastro-enterostomy or partial gastrectomy could have been performed. In nine cases, a previous gastro-enterostomy had been fol-

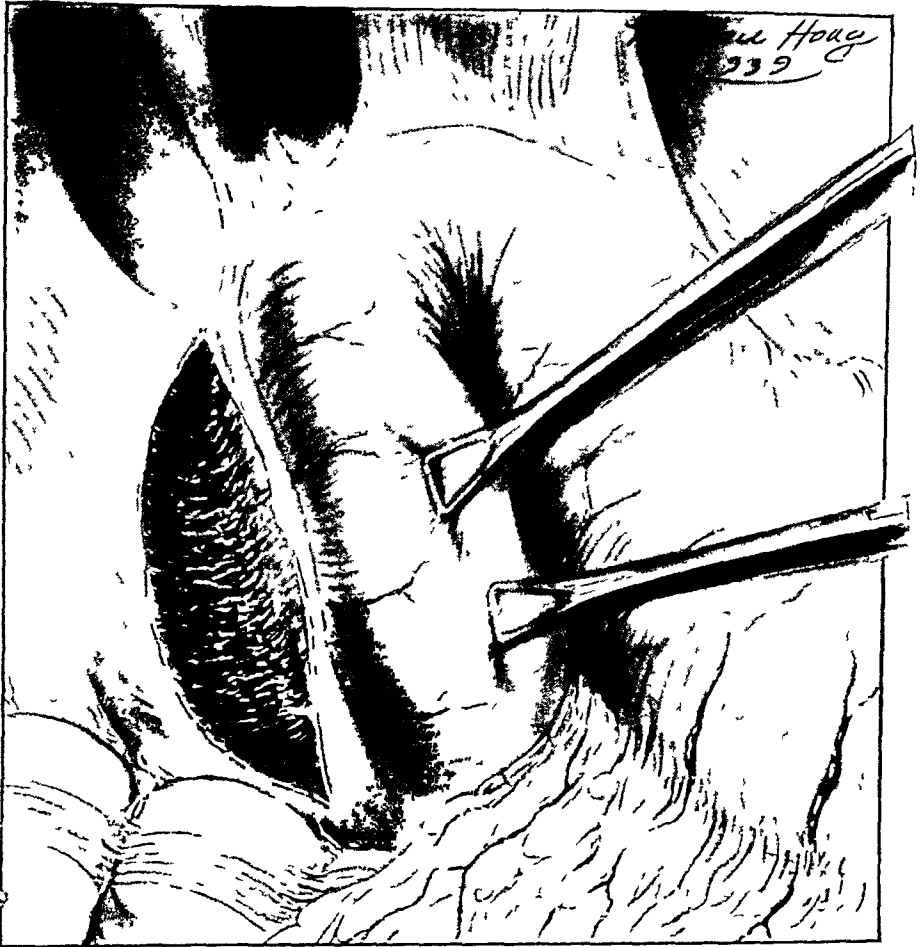


FIG 2—Mobilization of the duodenum facilitates its approximation to the antrum of the stomach without angulation or undue tension

lowed by marginal or jejunal ulcer and instead of performing a partial gastrectomy the gastrojejunal anastomosis was taken down the marginal or jejunal ulcer was excised and a lateral gastroduodenostomy was employed. A gastrojejunocolic fistula existed in two cases. The satisfactory results which followed in these cases justify conservative surgical procedures in many cases in preference to radical partial gastrectomy. Snell has directed attention to the element of mechanical difficulty as the result of deformity of the pyloric outlet produced by the operation of lateral gastroduodenostomy. Judging from my experience, the amount of such deformity is dependent upon how thoroughly the duodenum is mobilized. Worthy of emphasis is the fact that

in performing a lateral gastroduodenostomy it is necessary that the duodenum be carried over to the stomach instead of the stomach being drawn over to the duodenum (Figs 2 and 3) The operation is not applicable in all cases, by virtue of anatomic relationship variations, and should not be forced when deformity of the pyloric outlet or angulation of the duodenum below the anastomosis is likely to result



FIG 3—The anastomosis is made without clamps on either the stomach or the duodenum

To those surgeons who have abandoned gastro-enterostomy for duodenal ulcer or who employ the procedure with misgiving on account of the variable frequency with which in their experience marginal ulcer either as true gastro-jejunal or jejunal ulcer has occurred, lateral subpyloric gastroduodenostomy in certain cases should appeal To those who are not wholeheartedly committed to the theory and principle of partial gastrectomy for duodenal ulcer, the operation of gastroduodenostomy provides a conservative surgical procedure which at times may be employed with maximum assurance against recurrence or new ulcer formation at or about the stoma Likewise, the operation serves admirably as a secondary procedure in certain cases when an operation is necessary subsequent to a simple closure following an acute per-

foration, or in occasional instances of recurrent ulcer subsequent to pyloroplasty or gastro-enterostomy

REFERENCES

- ¹ Balfour, D C Gastroduodenostomy Its Indications and Technique ANNALS OF SURGERY, 67, 80-82, 1918
- ² Clute, Howard M, and Sprague, John S Gastroduodenostomy for Certain Duodenal Ulcers J A M A, 111, 909-915, September 3, 1938
- ³ Finney, J M T, Jr Pyloroplasty and Gastroduodenostomy Surgery, 2, 738-758, 1937
- ⁴ Flint, E R Further Experiences with Gastroduodenostomy Lancet, 1, 12, January 1, 1927
- ⁵ Graham, Roscoe, R Technical Surgical Procedures for Gastric and Duodenal Ulcer Surg, Gynec and Obstet, 66, 269-287, 1938
- ⁶ Graves, Amos M Combined and Separate Effects of Bile, Pancreatic Secretion and Trauma in Experimental Peptic Ulcer Arch Surg, 30, 833-853, 1935
- ⁷ Hill, Frederick, C, Henrich, Leo C, and Wilhelmj, Charles M Changes Produced by Various Operations on the Stomach Arch Surg, 31, 622-631, 1935
- ⁸ Jaboulay De la Gastro-duodenostomie Arch Prov de Chir, 1, 551-554, 1892
- ⁹ Kocher The Freeing of the Duodenum and Gastroduodenostomy Scot Med and Surg Jour, 13, 311-318, 1903
- ¹⁰ McCann, James C Experimental Peptic Ulcer Arch Surg, 19, 600-659, 1929
- ¹¹ Moynihan, Sir Berkeley Abdominal Operations W B Saunders Company, Third and Fourth Edition, 1915 and 1921
- ¹² Reinhoff, William Francis Infrapapillary Gastroduodenostomy by Mobilization with Retromesenteric Displacement of the Duodenum and Jejunum ANNALS OF SURGERY, 95, 183-197, 1932
- ¹³ Wilkie, D P D Indications for Surgical Therapy in Peptic Ulcer Brit Med Jour, 1, 771, May 6, 1933

EXPERIMENTAL PROOF OF THE OBSTRUCTIVE ORIGIN OF APPENDICITIS IN MAN*†

OWEN H. WANGENSTEEN, M.D., AND CLARENCE DENNIS, M.D.
MINNEAPOLIS, MINN.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF MINNESOTA MEDICAL SCHOOL, MINNEAPOLIS, MINN.

IN a preliminary study,¹⁰ reported two years ago, from observations made upon the exteriorized, unobstructed appendix, evidence was presented which suggested that the vermiform appendix of man secreted fluid. It was also shown, at that time, that obstruction of the cecal appendage of the rabbit was followed consistently by evidence of rapid fluid secretion. During the time that has intervened since then, these studies have been extended considerably. In the present communication evidence of the secretory capacity of the vermiform appendix of man will be cited.

The behavior of the appendix when obstructed temporarily will be described and factual proof of the reproduction of the pathologic picture of spontaneous appendicitis through the agency of obstruction will be presented.

Method—From studies made upon the obstructed cecal appendage of the rabbit and the vermiform appendix of the chimpanzee,¹¹ it was apparent that in order to adduce convincing proof of the secretory capacity of the appendix of man it was necessary to incannulate the obstructed exteriorized appendix. Unobstructed appendicostomies permitting incannulation had been established incidentally when colostomy was performed for malignant disease of the colon. Exteriorization of the appendix in this manner had been accomplished readily through a button-hole incision and did not complicate the operative procedure.¹⁰

In a patient presenting a carcinoma of the ascending colon, it was possible to exteriorize, with the blood supply intact, after the Bloch-Mikulicz principle, the greater portion of the right half of the colon and the terminal ileum. A few days later, when the exteriorized bowel had become fairly well covered with fibrin and effectual sealing of the wound had occurred, the base of the appendix was ligated securely. The attachment of a closed water system connected to a recording manometer permitted determination of the constant increase in intraluminal pressure. The manometer used required addition of 0.58 cc. of fluid to raise the pressure reading 100 cm. of water.

It was obvious that this type of case, permitting determination of the secretory capacity of the vermiform appendix, would not be encountered frequently. After considerable deliberation the method depicted in Figure 1 was worked out. When preliminary colostomy was being performed for malignancy of the large bowel or rectum prior to excision of the lesion the appendix

* Read before the American Surgical Association, Hot Springs, Va., May 11-12, 1939.

† The researches presented herewith were supported by a grant of the Graduate School of the University of Minnesota, and also by a grant for technical assistance by the Federal Public Works Administration, Project No. 665-71-3-69, Subproject No. 258.

was exteriorized and obstructed. Through a button-hole incision placed over the base of the cecum, the appendix was delivered and the cecum around the base of the appendix was anchored securely to the parietal peritoneum by a number of fine silk sutures, thus placing the appendix in an extraperitoneal position. The base of the appendix was ligated with plain catgut No. 00, a cannula was placed in the appendix and as soon as the patient was returned to his room attachment was made to a manometric recording system. After it was determined whether or not the obstructed exteriorized appendix developed an increase of intraluminal pressure, the closed system was broken and the cannula was attached to a small Wasseimann tube (atmospheric pressure).

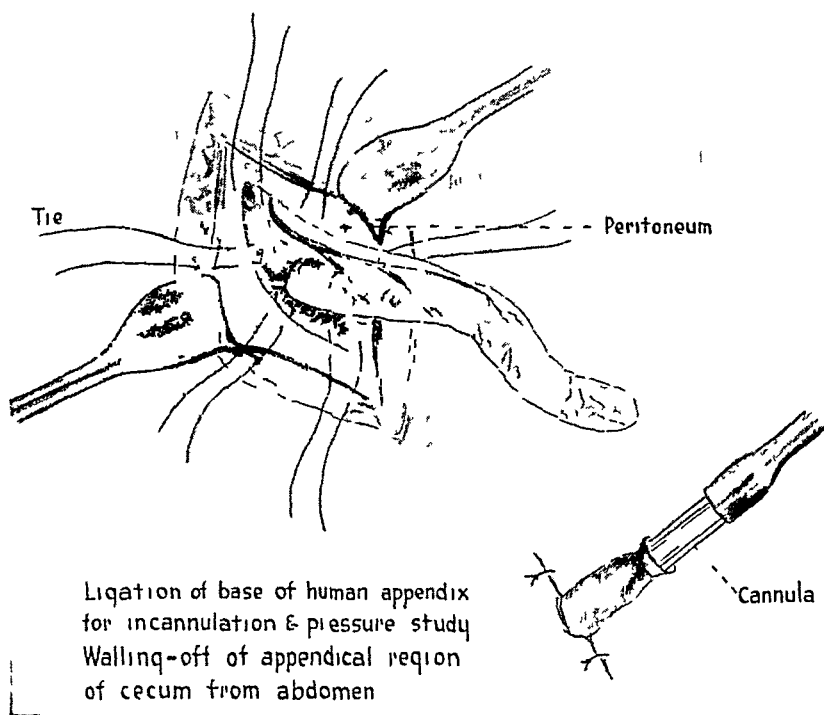


FIG. 1.—Technic of exteriorizing and obstructing an appendix as employed in this study for purposes of measuring the secretory pressure—a procedure performed coincidentally at the time of colostomy.

to note whether fluid could be collected. At this juncture a segment of the distal portion of the appendix was excised for purposes of histologic comparison with the segment removed as a control section at the time of operation. In a few instances leukocyte counts were made to determine whether increases of intraluminal pressure caused leukocytosis. No appendix was allowed to go on to perforation.

Before dismissal of the patient from the hospital the appendix was snipped off at the level of the skin and granulations grew over its orifice and skin soon covered the site where the appendix had been eviscerated.

In a few instances in which the appendiceal stump continued to secrete fluid, extraperitoneal excision of the residual segment beneath skin level was made.*

* No patient in the series came to harm through any of these manipulative procedures incidental to exteriorization of the appendix.

Results—The secretory activity of the obstructed appendicostomies is summarized in Table I. The cases have been grouped in the table with reference to the heights of secretory pressure attained. It is to be noted that the highest recorded pressure was 126 cm. of water, a level reached 22 hours after exteriorization and obstruction of the appendix in a man age 68. The next highest pressure recorded was 125 cm. of water, reached after 14 hours and 15 minutes in a man age 47. In a man, age 70, pressure of 92 cm. of water was reached 14 hours and 30 minutes after incannulation. The oldest patient in the series was age 75 (Case 20). No evidence of fluid secretion was noted. The appendix had a lumen but microscopic examination showed no evidence of mucosa. One patient in the series, R. A., Case 7 in the table, was age 29,

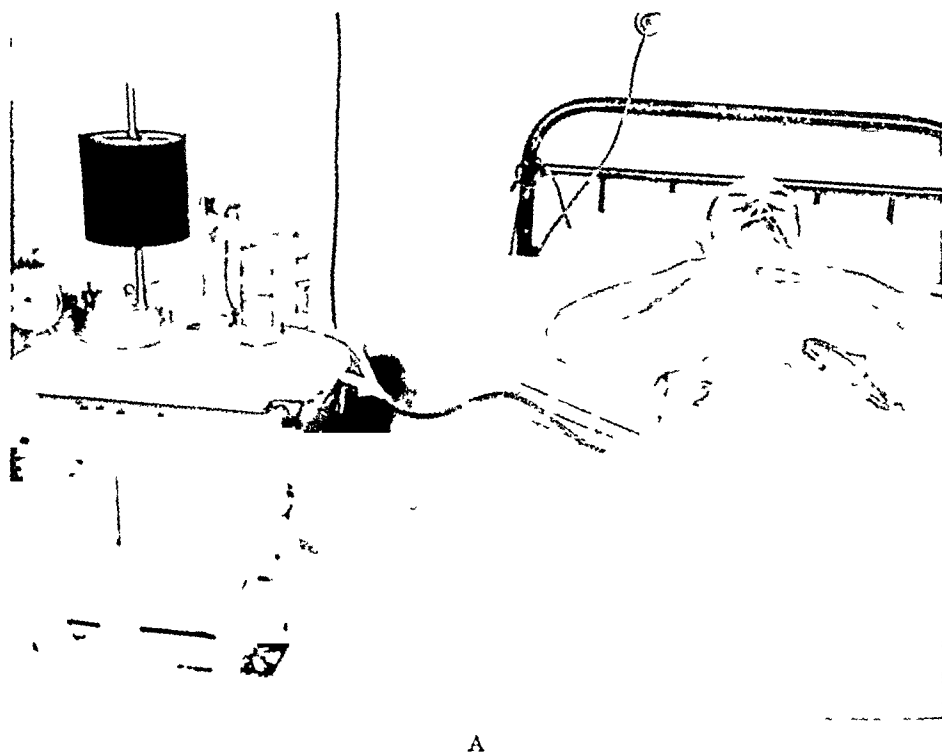


FIG. 2—A The patient and the manometric recording system for determining secretory pressure (Case 1, Table I)

G. L., Case 3, was age 33, the next youngest patient in the entire group was age 41. The average age for the group was 56.

No secretory pressure developed in three of the 22 exteriorized, obstructed appendixes. One of these was M. F., Case 20, age 75, referred to immediately above. In another, Case 22, G. B., age 53, whose cecum was exteriorized for polyposis, the blood supply of the appendix had been damaged in the manipulative maneuvers necessary to exteriorize the cecum and appendix and the negative result is essentially without significance. In the instance of a third patient, Case 21, A. C., age 61, the cannula had not entered the lumen and no secretory pressure was recorded. When the appendix was removed, however, exudate was found in the lumen.

In six other instances, however, a secretory pressure of less than 20 cm.

TABLE I
STUDIES OF SECRETORY CAPACITY OF OBSTRUCTED, EXTERIORIZED APPENDICES IN MAN

Case No	Initials, Univ Hosp No and Age	Maximum Pressure (Cm Water)	Time Required to Reach Maximum Pressure (Hrs)	Duration of Time Maximal Pressure Was Sustained (Hrs)	Total Fluid After End of Recording (Cc)	Period of Fluid Collection (Days)	Lapse of Time Between Onset of Experiment and Removal of Appendix	Histologic Study	
								Control Section	After Pressure
(1)	T W No 665959 M 68	126	22	2¾	3 5	2	25 hrs	Good mucosa	A D A *
(2)	O N No 662989 M 47	125	14¼	½	12 5	6	3 days	Good mucosa	A D A with necrosis
(3)	G L No 660228 F 33	114	35	14	3 25	5	50 hrs	Good mucosa	A D A
(4)	P G No 661973 M 70	92	14½	7½	1 5	2	48 hrs	Good mucosa	A D A
(5)	C P No 663022 M 56	90	16½	3	0 5	1	20 hrs	Good mucosa	A D A Loss of mucosa with fragmentation of muscle
(6)	U T No 666978 M 53	86	25½	0	?		Not removed	Good mucosa	No sections
(7)	R A No 661380 M 29	85	27	0	7 0	7	Not removed†	Good mucosa	
(8)	M K No 667935 M 54	60	3¼	5½	0 5	2	Not removed†	Good mucosa	No sections
(9)	W P No 660521 M 45	42	12	9	0	0	21 hrs	No sections	Mild A D A with exudate in lumen
(10)	F H No 661415 F 60	32	7	0	5 5	5	2 mos	No sections	
(11)	P S No 664561 M 73	24	24	0	0	—	Not removed†	Atrophic mucosa at distal end	
(12)	W H No 671573 M 53	20	(See text—pressure not allowed to rise above 20 cm)				Not removed	Good mucosa	
(13)	T C No 666127 M 66	20	24	0	0	2	Not removed	Much fat in submucosa	

ETIOLOGY OF APPENDICITIS

(14) A O	No 665635 F	53	17	20	0	7	2	8	Not removed	Fair mucosa with much lymphoid tissue	No sections
(15) E B	No 665350 M	58	15	18	0	0	—	—	Not removed†	Atrophic mucosa with much fat	No sections
(16) W B	No 665646 M	67	11	17	0	0	—	—	Not removed†	Atrophic mucosa with much fat	No sections
(17) A B	No 664251 F	41	8	2	24	7	4	13	13 days	No mucosa in control	No sections
(18) J S	No 667657 M	57	6	25	0	0	—	—	Not removed	No mucosa in control	No sections
(19) A T	No 662354 M	62	5	1	18	1	1	4	Not removed†	No mucosa in control	No sections
(20) M F	No 663863 M	75‡	0	—	—	—	—	—	Not removed†	No mucosa in control	No sections
(21) A C	No 653835 F	61‡	0	—	6 days	0	—	—	26 hrs	No mucosa in control	Mucus with leukocytes in lumen
(22) G B	No 661495 M	53§	0	—	—	1	0	2	6 days	No sections	No sections
										No sections	No sections

* A D A abbreviation for acute diffuse appendicitis
† Too short for removal
‡ Short mesentery, appendix under tension when exteriorized
§ Appendix devascularized during exteriorization

of water was recorded. In one of these, Case 17, A. B., age 41, the appendix had no mucosa. In the five others (Cases 14, 15, 16, 18 and 19), the segment of obstructed, exteriorized appendix was so short that on removal of the cannula, no specimen could be removed for biopsy.

In nine instances, the highest secretory pressure exceeded 40 cm. of water, in seven of these the pressure was sustained above 85 cm. In four instances, pressures intermediate between 20 and 40 cm. of water attended obstruction of the exteriorized appendix. In one of these, Case 12, W. H., age 53, the pressure was not allowed to mount over 20 cm. of water. As soon as that level of pressure was reached, the recording level was lowered to zero by re-

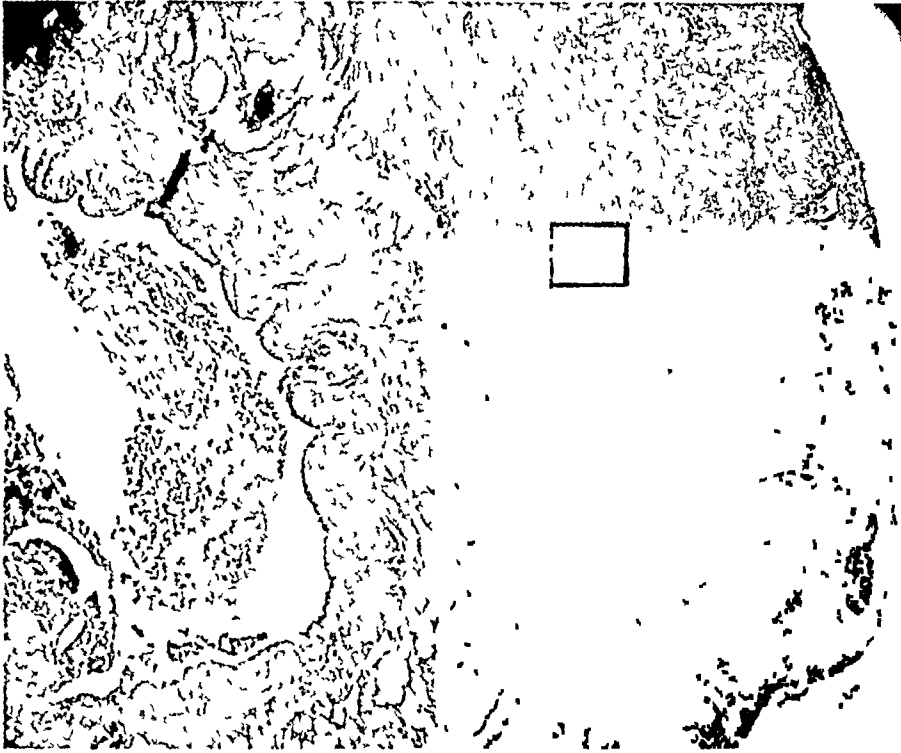


B

FIG. 2—B The control section—cut from the distal end of the appendix at the time the exteriorization was performed (X60)

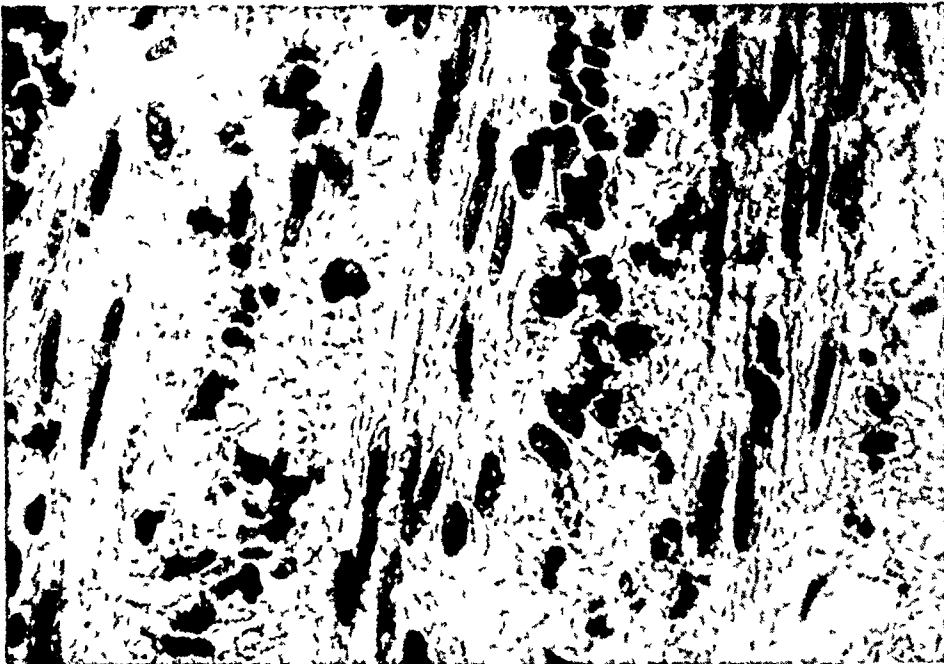
moval of fluid from the system by an aspirating syringe. On the first occasion, it took but 30 minutes for the level of 20 cm. of water pressure to be developed. After a wait of 20 minutes, it took 50 minutes to develop the same level of secretory pressure. After an interval of 24 hours, the level of 20 cm. pressure was reached in 18 minutes, on the third day it took 80 minutes and the same amount of time on the fourth day.

Discussion—These data support the thesis that the vermiform appendix of man when obstructed, will develop a secretory pressure in the majority of instances which will threaten the viability of the appendiceal wall. It is to be noted, however, that there are instances in which no evidence of secretory pressure attends luminal obstruction. Such appendices undoubtedly would tolerate luminal obstruction without hazard to their owners. The instance of W. H., Case 12 suggests that luminal obstructions which are survived di-



C

FIG 2—C After 25 hours of pressure ($\times 30$) The square indicates the site from which D was taken. There is a diffuse cellular infiltrate with exudate in the lumen. The fat in the submucosa is also apparent.



D

FIG 2—D A free exudation of polymorphonuclear cells has occurred into the muscular layer ($\times 500$). (The print has been turned to include visualization of a greater length of the muscle layer.)

minish the secretory capacity of the appendix. It is apparent, not alone from the small amount of fluid secreted by the normal appendix but by instances in which no evidence of fluid secretion was obtained, as well by the observations made on W. H., Case 12, cited above, that the balance between secretion and absorption, though weighted in the favor of the former, is poised on a somewhat narrow margin.

In the main, a fairly definite correlation was found to exist between normal microscopic appearance of the mucosa in the control section and the development of a high secretory pressure. This factor would appear to be the most significant item in determining whether an obstructed appendix will secrete fluid. Obliteration or connective tissue replacement of the luminal mucosa is certain to be correlated with a lack of secretory capacity in the vermiform appendix. The presence of fat in the submucosa, if the mucosa itself is normal, does not militate against the development of high secretory activity (Fig. 2C). An abundant lymphoid tissue, beneath an atrophic mucosal layer, does not assure rapid fluid production (A. O., Case 14, Table I).

*Appendicostomy—with base tied
Closed System
Case of T. W.
(Case I, Table I)*

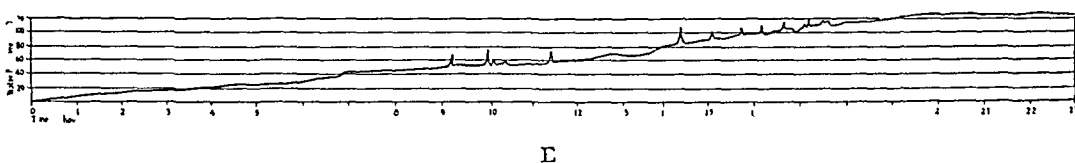


FIG. 2—E Retraced pressure record—the slope of the rising pressure is indicated. A pressure of 126 cm. water was reached 22 hours after obstruction.

It would appear, therefore, that the more normal the appendix, the more likely it is when obstructed to secrete fluid rapidly, pyramiding the intraluminal pressure with resultant anoxic effects upon the appendiceal wall. The disintegration of the wall of the appendix eventuating in perforation or gangrene is owing in part to the fluid transudation occasioned by the resistance of the high intraluminal tension and in part by cellular migrations into the wall as well as through bacterial invasion. A normal appendix which will withstand an intraluminal tension of approximately three atmospheres of pressure without rupturing, immediately after excision will perforate at very low values (20 to 70 cm. of water pressure) if it had been subjected to prolonged maintenance of sustained intraluminal pressures within the range of secretory pressures recorded in Table I. It is to be recalled that the luminal capacity of the normal appendix at atmospheric pressure is essentially zero, and that at 60 cm. of water pressure the usual luminal volume of the normal appendix is about 0.5 cc.¹⁰

Whereas, in an earlier study,¹⁰ the impression was lent on the basis of a study of the secretory behavior of the cecal appendage of the rabbit that catharsis accelerated fluid secretion, a more adequately detailed controlled study of this item suggests that neither fluid secretion nor perforation is hurried by purgation.⁴ In the rabbit, obstruction of the cecal appendage will be followed

ETIOLOGY OF APPENDICITIS

by perforation in 75 per cent of instances within 10 hours after ligation of the base The administration of cathartics induces movements of the appendix

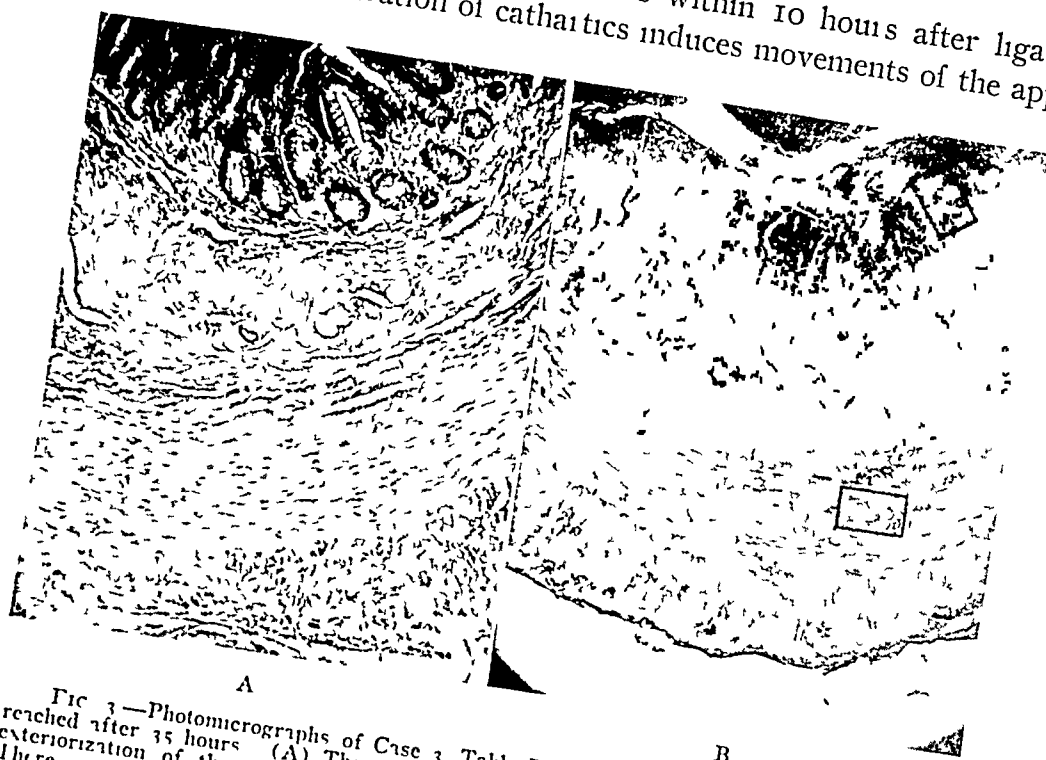


FIG 3—Photomicrographs of Case 3 Table I A pressure of 114 cm of water was reached after 35 hours (A) The control section removed at the time of obstruction and exteriorization of the appendix (x65) (B) After 50 hours of sustained pressure there is a diffuse cellular reaction throughout the wall—some exudate is present in the lumen (x65)

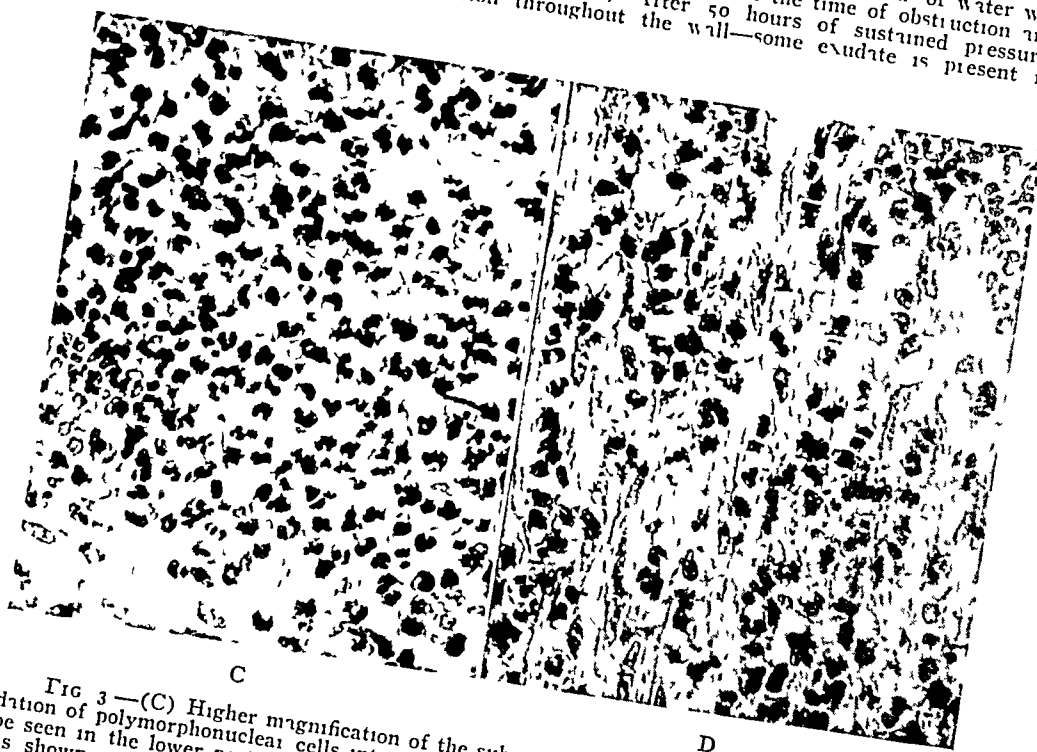


FIG 3—(C) Higher magnification of the submucosa as shown in B (x550) The exudation of polymorphonuclear cells into the submucosa is apparent A few muscle cells may be seen in the lower portion of the section (D) Higher magnification from lower square as shown in D (x550) The section is turned on the side to permit inclusion of a greater portion of the muscle layer Many polymorphonuclear cells may be seen scattered among the spindle shaped muscle nuclei

which preclude effectual sealing-off at the site of perforation by adjacent coils of intestine or other peritoneal surface 4

Histologic Study of Obstructed Appendices—It is to be conceded freely, that the vermiform appendix exteriorized upon the abdominal wall is not a properly controlled experiment for histologic observations. Every appendix exteriorized in this manner, whether or not it develops a high secretory pressure, exhibits evidence of thickening of the peritoneal tunic of the appendix (serositis). In two unobstructed, exteriorized appendices, employed for purposes of control in which a catheter was left in the lumen, in one instance (case of C S, age 65, U H No 670933) for six weeks before excision of the specimen and in the other 12 days (case of B N, age 33, U H No



FIG. 4.—Section of a gibbon's obstructed appendix after 22 hours of incannulation. The highest pressure reached was 19 cm of water—a pressure sustained for less than one hour. There is evidence of serositis. Otherwise the section is normal.

660885), the lumen and mucosa in each instance were normal. Both exhibited marked serosal thickening and cellular infiltration was apparent in the muscle layer.

Our best controlled observations were upon the obstructed appendices¹¹ of apes. Here, it was possible to leave the obstructed appendix within the peritoneal cavity or at least well beneath the skin. In the chimpanzee which develops with luminal obstruction a secretory pressure not unlike man or the rabbit, a diffuse cellular infiltration of all the walls attends obstruction. In

the gibbon, on the contrary, in which the highest pressure attained was 20 cm., and not long sustained, luminal obstruction was not attended by leukocytic invasion of the walls (Fig. 4). A mild serositis only attended the exteriorization.

As has already been related in the statement concerning the results of luminal obstruction of the vermiform appendix of man, the best determinant of whether an appendix will secrete fluid and develop the histologic picture of acute diffuse appendicitis consequent upon obstruction, is the presence of a normal mucosa. All instances in which high secretory pressures followed obstruction were attended by the histologic pictures of acute diffuse appendicitis. The histologic study of two of these (Cases 1 and 3, Table I) is shown in Figures 2 and 3. The details of the histologic findings are listed in Table I.

Dr. R. E. Bunge,¹ of this Clinic, has made cell counts of the exudate found within the lumen of appendixes exhibiting no demonstrable evidence of inflammation within its wall as well as upon the exudate within the lumina of appendixes exhibiting definite evidence of acute diffuse appendicitis. Similarly, he has made cell counts upon the exudate appearing in the lumina in a number of the patients in this series whose appendixes were obstructed and exteriorized. It is well known that cells are extruded constantly into the intestinal canal and the exfoliation of epithelial cells from the appendiceal mucosa as well as extrusion of white blood cells through the intact appendiceal mucosa is generally accepted as a constantly occurring phenomenon^{6, 7, 9}.

Bunge observed that this exudate, which may be observed not uncommonly within the lumen of an appendix, the wall of which fails to exhibit evidence of inflammation, possesses regularly a predominantly lymphocytic character.³ In a group of seven such cases in the appendixes of man, out of 100 cells within the lumen the average lymphocytic count was 90. In instances of spontaneously occurring appendicitis, on the contrary, a count of the luminal exudate showed invariably a definitely predominant polymorphonuclear leukocytosis. In a group of 13 such instances, the average polymorphonuclear count on the luminal exudate was 86 cells out of every 100 counted. Similarly in a group of six obstructed, exteriorized appendixes in which fluid secretion was active, the cell counts on the luminal exudate showed the average polymorphonuclear count to be 82 cells out of every 100 cells counted. It is apparent, therefore, that the same type of cellular response attends obstruction of the exteriorized appendix as is observed in instances of spontaneous appendicitis. The exudation of polymorphonuclear cells into the muscle layer in obstructed exteriorized appendixes is apparent in Figures 2 and 3.

Effect of Appendiceal Obstruction Upon Production of Pain, Fever and Leukocytosis—In a number of instances, careful notations were made with reference to pain or discomfort attending obstruction of the exteriorized appendix. The presence or absence of pain in these cases was difficult to determine in most cases or was rendered actually inconsequential by the administration of opiates to relieve postoperative pain. In the main, it would appear that a colicky pain not unlike that observed in spontaneously occurring appen-

ditis could be reproduced by luminal obstruction in those patients whose appendixes secreted fluid actively and developed a high secretion pressure. In Case 5, Table I, the details of which are listed below, it is apparent that the pain could be reproduced almost at will by elevating or lowering the intraluminal tension within the appendix. It is obvious, however, after a fairly high intraluminal pressure has been sustained for some time, that the occurrence of pain may be modified in proportion to the degree with which the circular muscle of the appendix resists distention.

Both fever and a polymorphonuclear leukocytosis were fairly constant accompaniments of the intraluminal pressure which attended obstruction of the exteriorized appendix. It is difficult, of course, to evaluate with exactness the temperature and leukocyte response to the performance of the colostomy.

Determination of how the factors of pain production, fever* and leukocytosis were influenced by obstruction of the appendix was made in a large number of the group. Observations noted at the time of the recording of the secretory pressures with reference to the occurrence of pain, fever and leukocytosis is indicated in a few of the actively secreting appendixes as listed below.

Case 1, Table I—T W, age 68. Obstruction and exteriorization of a rather long and free appendix. Insertion of cannula for recording pressure.

1 day prior to operation—W B C, 7,700, P M N, 62%

At start of record—Temperature, 99.2° F

After 4 hrs—Temperature, 99.6° F, pressure, 22 cm water

After 12 hrs—Temperature, 99.8° F, pressure, over 60 cm water

Waves occur with peaks every five to ten minutes (peaks up to 80 cm water pressure)

After 14 hrs—Pressure, 78 cm water. Waves becoming smaller, W B C, 15,600, P M N, 82%

16 hrs after exteriorization—Pressure, 100 cm water, temperature, 99.4° F. Appendix pale and distended, no serosal discharge, circulation present, no pain.

At 18 hrs—Pressure, 115 cm water. Waves smaller and peaks less high (up to 125 cm water)

At 20 hrs—Pressure, 125 cm water, temperature, 100° F. Waves even smaller (see Fig. 2E)

At 22 hrs—Pressure, 126 cm water, W B C, 15,000, P M N, 89%

Pressure recording stopped and pressure removed. The patient had denied pain earlier, but on removal of the pressure he stated that he was suddenly relieved of a dull aching pain in the right lower quadrant. This dull ache was not reproduced, however, by raising the pressure again.

38 hrs—W B C, 13,000, P M N, 77%. There was a slight elevation of temperature for two days after release of pressure.

Ultimate Outcome—Dismissed from hospital and returned later for posterior excision.

Case 2, Table I—O N, age 47. Obstruction and exteriorization of appendix followed by incannulation for recording pressure.

At 7 hrs after start of record—Pressure, 80 cm water with 4 cm waves, temperature, 99.2° F, W B C, 24,000, P M N, 86% (waves synchronous with pulse)

At 9 hrs—Appendix looks tense. The larger vessels on the surface were engorged, but the areas between were blanched. Patient denied pain even to leading questions.

* All temperature determinations are rectal.

At 14 hrs—Pressure, 125 cm water with 2 cm waves synchronous with pulse, W B C, 16,000, P M N, 86% Appendix more blanched and there were fewer vessels holding blood The volume of the appendix at this time was 125 cc The temperature rose to a maximum of 101° F at 21 hrs, then returned to normal in a few hours (Fig 5)

Ultimate Outcome—Carcinoma inoperable Radon insertion

Dismissed from hospital

Case 3, Table I—G L, age 33 Obstruction and exteriorization of appendix followed by incannulation for recording pressure Preliminary volume-elasticity determination showed a leak occurring between 80 and 120 cm of water pressure (base not tied tight)

At 3 hrs—Pressure, 22 cm water, temperature, 99.6° F

At 12 hrs—Pressure rise ceased and pressure leveled off abruptly, presumably due to leakage into cecum or seepage, pressure 97 cm water Slight peristaltic waves every few minutes and also pulse waves

At 15 hrs—Pressure, 96 cm water waves disappearing, temperature, 100° F

At 18 hrs—Pressure, 98 cm water, W B C, 11,800 Patient has no complaints—occasionally questioning elicits confession of vague lower abdominal soreness "like a stomach ache"

At 19 hrs—Pressure, 99 cm water, temperature, 99.6° F Pulse waves rise 1 to 1½ cm

At 20 hrs—Pressure, 101 cm water There are occasional peaks to about 120 cm due to movements of the patient and followed by a gradual fall to a lower level as if some fluid had been lost

At 23 hrs—Pressure, 95 cm water, temperature, 100.2° F

At 26 hrs—Pressure, 102 cm water, W B C, 9,800, P M N, 89%

At 27 hrs—Pressure, 104 cm water, temperature, 100.4° F

At 28 hrs—Pressure, 110 cm water

At 29 hrs—Pressure, 106 cm water Lower abdominal discomfort

At 30 hrs—Pressure, 105 cm water, W B C, 10,200, P M N, 86%

Waves bigger Appendix more blanched than earlier

No necrosis evident

At 42 hrs—Pressure, 108 cm water Almost no waves now

W B C, 8,300 There was a pressure peak lasting ten minutes after taking blood for W B C

At 44 hrs—Pressure, 96 cm water, temperature, 100.8° F

At 47 hrs—Pressure, 100 cm water, temperature, 101.2° F Still vague abdominal aches

At 49 hrs—Pressure, 105 cm water, W B C, 13,000, P M N, 94%

At 49½ hrs—Pressure released No change in abdominal pain Volume elasticity determination showed no demonstrable stretching of the lumen

Still 0.17 cc at 100 cm

At 50¼ hrs—Temperature, 98.6° F

At 62 hrs—Temperature, 100° F, W B C, 7,200, P M N, 92%

Ultimate Outcome—Colostomy was performed for obstruction due to spread of cancer of cervix uteri

Case 5, Table I—C P, age 56 Obstruction and exteriorization of appendix followed by incannulation for recording pressure

After 16 hrs—The pressure had risen to 90 cm water with waves up to 95 to 130 cm coming every 10 to 15 minutes, the high points being climaxed by a spike Careful questioning of the patient showed that he had sharp severe pains coming just as the pressure commenced to rise for each of these peaks, reaching its climax about two-thirds of the way up to the peak and ceasing just as the pressure commenced to drop This was right lower quadrant pain Just as it

ceased each time (after lasting 20 to 30 seconds) the patient had a pain in the left side in the region of the Mikulicz exteriorization of the carcinoma. Slightly more severe and evidently of the same nature (Fig 6)

Ultimate Outcome—Bloch Mikulicz resection of carcinoma of sigmoid. Recovery

Case 6, Table I—U T, age 53. Obstruction and exteriorization of appendix followed by incannulation for recording pressure. The mesentery was too short to allow stretching the organ out straight and it was, therefore, kinked on itself in and just above the muscle layers of the abdominal wall.

At start—volume-elasticity determination D 4 cc at 120 cm water pressure

After 16½ to 18½ hrs—Pressure rose from 19 to 72 cm water in a few small and one large jump suggesting that at this point fluid passed the kink

At 19½ hrs—Pressure, 73 cm water, temperature, 100.2° F

Pulse waves visible from this point onward

At 20½ hrs—Pressure, 74 cm water, W B C, 13,000, P M N, 82%

At 23½ hrs—Pressure, 85 cm water, temperature, 102° F. No pain at any time

At 25½ hrs—Pressure, 86 cm water, temperature, 101.6° F, W B C, 15,000

Pressure released, no change in sensations resulted

Volume-elasticity determination at end of pressure recording—0.13 cc at 120 cm of water pressure

At 29 hrs—W B C, 11,000, P M N, 76%

At 32 hrs—Temperature, 101.6° F

At 36 hrs—Temperature, 100.8° F

At 40 hrs—Temperature, 100° F

Ultimate Outcome—Failed to return for posterior excision of rectum

Case 8, Table I—M K, age 54. Obstruction and exteriorization of appendix followed by incannulation for recording pressure

Barium in lumen from 24 hrs before start—W B C, 10,000

After 6½ hrs—W B C, 13,200

At 8¾ hrs—Pressure, 51 cm water

At 24 hrs—Pressure, 45 cm water

At 25 hrs—W B C, 12,800

At 26 hrs—Waves begin to appear. Peaks come every 20 mins and there are sharper waves between. The basal level rose gradually to 56 by 30 hrs

At 30 hrs—Sudden drop in pressure to 26 cm with loss of waves suggesting rupture. Temperature, 101° F. No leak, however

At 32½ hrs—Pressure, about 20 cm. W B C, 8,600. Pressure released. The temperature returned to normal in a few hours thereafter

Ultimate Outcome—Resection of carcinoma of sigmoid colon. Recovery

The Secretory Activity of the Obstructed Cecal Appendage in Animals—

Rabbit—Two years ago, it was reported¹⁰ that rupture of the rabbit's cecal appendage attended luminal obstruction quite regularly. In about 75 per cent of instances perforation occurs within 10 hours after ligation of the base. The highest secretory pressure that has been observed to date (136 cm of water) followed luminal obstruction of the cecal appendage in the rabbit. A large number of observations have been made upon rabbits, and failure to secrete has not yet attended obstruction.⁴ The character of the secretions may be modified, however, by regulating the pressure at which secretion occurs.⁸

Other Animals—The secretory behavior of the cecal appendage of a large number of other animals has been investigated, including most of the domestic animals as well as fowl, carnivorous mammals, rodents and monkeys. No

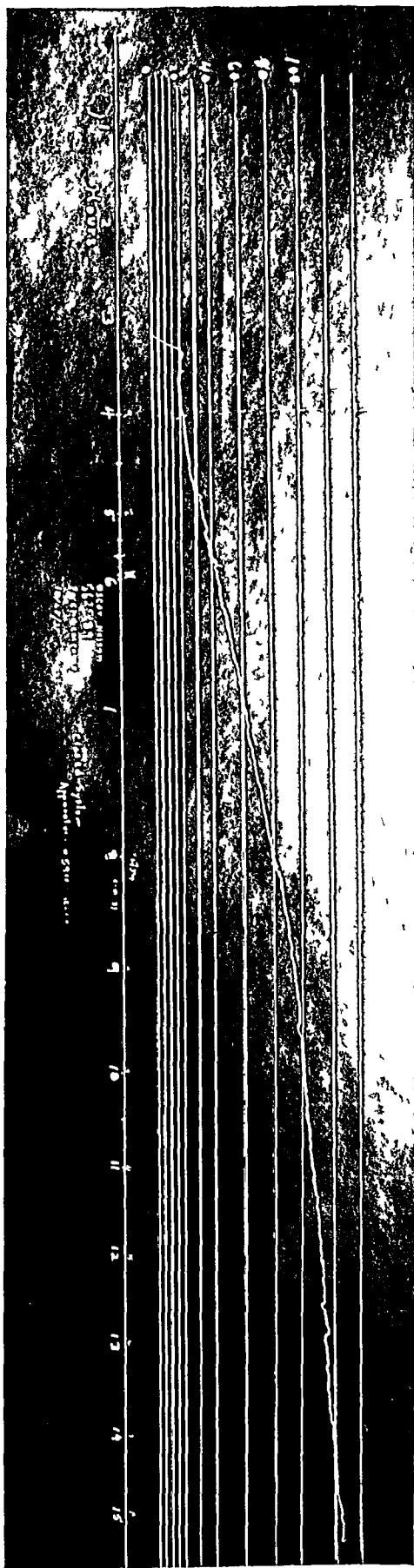


FIG 5.—Pressure tracing of O.N., Case 2, Table I. A pressure of 125 cm water was reached 14 hours and 15 minutes after obstruction.

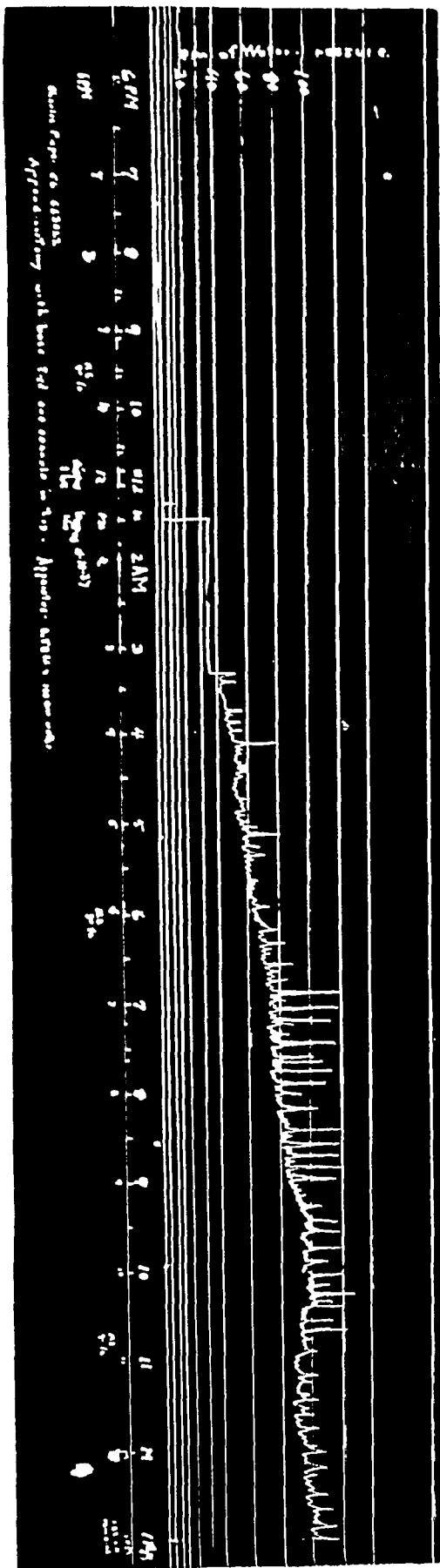


FIG 6.—A Pressure tracing of C.P., Case 5, Table I. A pressure of 90 cm water was reached 16 hours and 30 minutes after obstruction.

evidence of secretory activity in the obstructed cecal appendage was noted in any of these³

Anthropoid Apes—The secretory activity of the vermiform appendix has been studied in two species of anthropoid apes, the gibbon and chimpanzee¹¹ The highest secretory pressure observed in two gibbons was 19 cm of water and in neither instance was this maximal pressure sustained for long

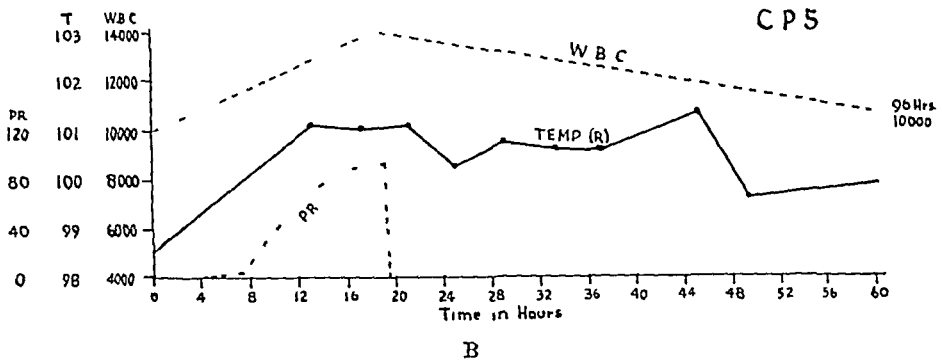


FIG 6—B Chart indicating the leukocyte and temperature response incident to obstruction (See details of case record No 5)



A

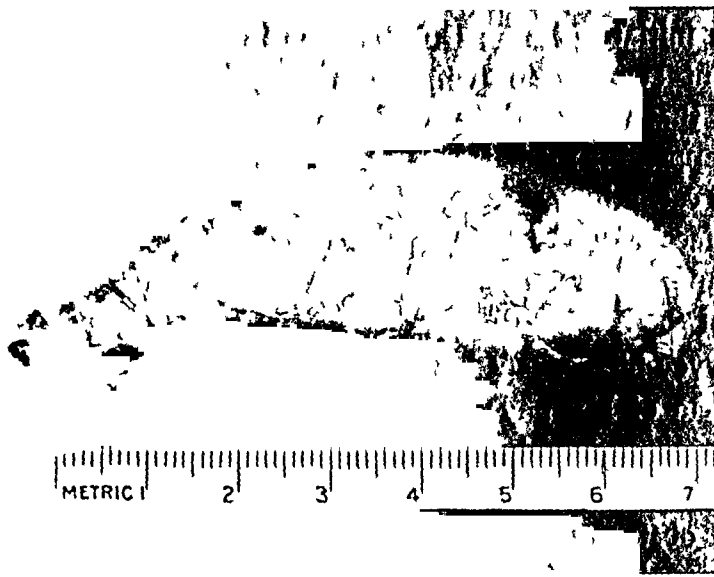
FIG 7—A The obstructed cecal appendage of a rabbit from which fluid has been collected in a balloon. Two hundred cubic centimeters was collected in five days. The appendage is normal grossly and microscopically.

The vermiform appendix of the chimpanzee, on the contrary, exhibits a secretory pressure not unlike that of man and the rabbit. The highest pressure recorded in the obstructed appendixes of three chimpanzees was 106 cm of water.

The Nature of the Fluid Secreted by the Obstructed Appendix—Because of the small amount of fluid collectable from the obstructed vermiform

appendix of man, extensive observations on its nature have not been possible. The determinations made have been upon rather small quantities of fluid as is apparent from inspection of Table I. These would suggest that mineral salts such as calcium and phosphates may be present, as well as digestive enzymes. It is necessary, however, to rule out bacterial activity before concluding that digestive enzymes are present in the fluid.

Extensive observations have been made on the fluid secreted by the obstructed cecal appendage of the rabbit, however. About 20 cm of fluid may be collected every six hours. Digestive enzymes are usually present in the fluid as it is collected in a small balloon within the rabbit's abdomen. After Berkefeld filtration to remove bacteria, however, no trace of proteolytic or other digestive enzymatic activity persists.⁸



B

FIG 7—B Obstructed cecal appendage of a rabbit. Perforation occurred 5 hours and 18 minutes after recording was commenced, a pressure of 69 cm water having been reached. Other areas of necrosis are apparent. This appendage showed evidence of diffuse cellular infiltration with areas of necrosis microscopically (Reproduced from ANNALS OF SURGERY, 106, 927, 1937)

Is the Fluid a True Secretion or a Filtrate?—Whereas, no substance has been identified in the fluid which would stamp it definitely as a secretion of the mucosa of the appendix, there is every reason to believe that this fluid is secreted by the mucosa. First, fluid may be collected from the obstructed appendix at atmospheric pressure in both man and the rabbit (Fig 7). Obstruction of the base of the cecal appendage in animals in which no secretory pressure develops is unattended by fluid secretion. Secondly, pressures attending obstruction of the appendix in man (126 cm water or 92.6 Mm mercury), chimpanzee (106 cm water or 77.8 Mm mercury) and the rabbit (136 cm water or 100 Mm mercury) have been observed to approach the systolic level of blood pressure. It has been remarked already that appendixes possessing an atrophic mucosa failed to exhibit evidence of fluid secretion (Table I). Observations made by Dr C. J. Bellis,¹ in this clinic,

on the intraluminal pressures in spontaneously occurring appendicitis (obstructive) and the interstitial tissue pressures indicate that the intraluminal pressure distal to the obstruction, is higher in instances of acute appendicitis than is the interstitial pressure

Clinical Significance of the Secretory Capacity of the Appendix—The observations related above serve to emphasize the great importance of obstruction in the genesis of spontaneous appendicitis in man. The histologic picture of spontaneous diffuse appendicitis has been reproduced through the agency of obstruction alone. In the cecal appendage of the rabbit, all the varieties of appendicitis recognized by the pathologist from mere subserosal leukocytic invasion to gangrene or perforation may be produced by luminal obstruction.

That the rich lymphoid tissue of the vermiform appendix of man may play a rôle in initiating luminal obstruction in infections or other conditions which augment swelling in lymphoid tissue, is understandable. It would appear likely that this is the probable mechanism by which the lymphoid tissue of the appendix mediates its influence in causing appendicitis.

The usual causative agent in demonstrable obstruction of the appendiceal lumen is the fecolith.² How in turn it originates, still demands explanation.

It would appear necessary that the pathologist consider anew the obstructive concept of the origin of appendicitis. It is even more important that the clinician resurvey his concept of the early symptoms and findings of appendicitis. The dicta of Murphy, namely, pain, nausea and vomiting, abdominal tenderness, fever and leukocytosis, have been accepted almost universally as clinical desiderata of the disease. Appendicitis, however, is essentially a closed-loop obstruction in which the only early findings may be intermittent crampy pain and local tenderness. Elevation of temperature, quickening of the pulse and leukocytosis may not be in evidence until the anoxic effects of increased intraluminal pressure have set the infective characters of the disease in motion.⁹ Finally, in order that the unwarranted mortality of the disease may be reduced more effectually, it would appear necessary to liberalize the indications for excision of the vermiform appendix. Appendicitis is probably still the most important of all surgical diseases. It ranks high as a cause of death and should be looked upon as a problem of the public health.⁹

CONCLUSIONS

The secretory activity of the vermiform appendix of man, possessing a normal mucosa, has been established. Such an appendix when obstructed and exteriorized may develop a secretory pressure approaching systolic blood pressure. The histologic picture of acute diffuse appendicitis has been produced in man by obstructing the exteriorized appendix. Appendices having an atrophic mucosa fail to exhibit evidence of fluid secretion when obstructed. It appears likely that the chief inciting agency in bringing about appendicitis

in man is obstruction of an appendix in which the mucosa possesses the normal secretory capacity

REFERENCES

- ¹ Bellis, C J Unpublished data
- ² Bowers, W F A Study of Appendicitis, with Especial Reference to Its Pathogenesis, Bacteriology and Healing (Ph D Thesis) ANNALS OF SURGERY In Press
- ³ Burge, R E, Dennis, C, and Wangensteen, O H The Histologic Picture of Experimental Appendical Obstruction in Rabbit, Ape and Man In Press
- ⁴ Dennis, C, Burge, R E, and Wangensteen, O H The Secretory Capacity of the Cecal Appendage of Various Animals In Press
- ⁵ Dennis, C, Burge, R E, Varco, R, and Wangensteen, O H Unpublished data on the production of appendicitis in the rabbit
- ⁶ Jassinowsky, M A Uber die Herkunft der Speicheldruesen Frank Ztschr f Path, 31, 411, 1925
Jassinowsky, M A Uber die Emigration auf den Schleimhauten des Verdauungskanal Frank Ztschr f Path, 32, 238, 1925
- ⁷ Sinelnikoff, E I, and Jassinowsky, M A Uber die Leukozytenemigration im Isolierten Abschnitt des Dunndarms Beim Hunde Frank Ztschr f Path, 35, 150, 1927
- ⁸ Varco, R, and Wangensteen O H Unpublished data
- ⁹ Wangensteen, O H The Genesis of Appendicitis in the Light of the Functional Behavior of the Vermiform Appendix Proc Inst Med, Chicago, 12, (No 11), 1939 (Fifteenth McArthur Lecture)
- ¹⁰ Wangensteen, O H, Burge, R E, Dennis, C, and Ritchie, W P Studies in the Etiology of Acute Appendicitis ANNALS OF SURGERY, 106, 910, 1937
- ¹¹ Wangensteen, O H, and Dennis C The Production of Experimental Acute Appendicitis (with rupture) in Higher Apes by Luminal Obstruction In Press

ILEOCOLOSTOMY WITH EXCLUSION*

LEON GINZBURG, M D , RALPH COLP, M D , AND MARCY SUSSMAN, M D
NEW YORK, N Y

FROM THE SURGICAL SERVICE OF THE MOUNT SINAI HOSPITAL, NEW YORK, N Y

Two of the most important developments in intestinal surgery during the last decade have been the increasing recognition of localized inflammatory disease of the terminal ileum and colon, and the trend in some surgical clinics toward stage procedures in the operative management of colonic neoplasms. As a result, ileocolostomy with exclusion is being more frequently performed either as a preliminary or definitive operation in inflammatory disease, and as a first-stage procedure in the resection of benign and malignant lesions of the right colon. The following communication is based upon the study of 32 cases of ileocolostomy with exclusion. This includes 16 cases of ileosigmoidostomy for regional ileitis and proximal regional hypertrophic colitis, three cases of ileotransverse colostomy for regional ileitis, and 13 cases of ileosigmoidostomy with ileocolic resection for malignancy of the right and transverse colon. Palliative anastomoses were not included as the period of survival was too short. These enterocolonic anastomoses were all routinely accompanied by transverse section of the ileum distal to the site of the anastomosis in order to completely exclude and short-circuit the intestinal flow from the diseased bowel. The technic followed has been to divide the terminal ileum between Payr clamps, carrying the incision well into the mesentery of the small bowel in order to secure the necessary independent mobility of the proximal and distal segments. Both ends were then closed by suture and continuity of the bowel was restored by a side-to-side enterocolostomy. No special attempt was made to perform an isoperistaltic anastomosis, the respective segments being placed along the axis in which they naturally lay. In lesions affecting the right and transverse colon, the ileum was divided about eight to ten inches from the ileocecal junction, great care being taken to preserve the integrity of the ileocolic vessels. In cases of nonspecific ileitis, the small intestine was divided through presumably healthy bowel at a point well proximal to the most oral segment presenting visible evidence of disease.

The operation as outlined above has always been preferred to ileocolostomy in continuity. The latter procedure is not infrequently complicated by trapping and stasis, factors which may produce marked distention and tension ulcerations of the loop of intestine between the enterocolic stoma and the area of diseased bowel. This complication, which may give rise to severe symptoms, has been emphasized by Estes and Holm,¹ and was observed twice in the course of secondary operations in which an ileocolostomy in continuity had been previously performed. Other disadvantages of this procedure are that secondary resections may be more difficult from a technical standpoint.

* Read before the American Surgical Association, Hot Springs, Va, May 11, 12, 13, 1939

Furthermore, in the presence of ileal or cecal fistulae intestinal leakage would still continue freely because the intestinal current had not been completely diverted.

The original gratifying results with ileocolostomy with exclusion were achieved in cases in which this operation had been primarily intended as a preliminary to later resection. The clinical improvement in many of these patients was so marked and the disappearance of intra-abdominal inflammatory masses and cutaneous fecal fistulae was at times so rapid, that we came to the conclusion that contemplated resection for inflammatory diseases should usually be performed in stages. The improvement following this relatively simple procedure has proven to be so great in numerous instances that resection in these patients has been indefinitely postponed.

Objections to ileocolostomy with exclusion have been raised on a number of grounds. The fear has been voiced that obstruction might produce sufficient back pressure to imperil the suture line of the distal excluded ileum. This complication has not been encountered in the present series. First, inflammatory disease rarely goes on to produce a complete obstruction. Second, the secretion of mucus and fluid requires only a very small channel to evacuate itself. In addition, malignant lesions of the right colon are rarely completely obstructive and in those cases in which acute obstruction has occurred preliminary cecostomy has been performed. In cases of subacute obstruction in which there really is a doubt, the distal ileal loop may be brought out on the abdomen through a counter incision in a manner similar to the distal segment in the Lahey operation for carcinoma of the rectum.

Another danger which has been pointed out, is distention and possible perforation of the blind loop of ileum used in the side-to-side anastomosis. This danger is not peculiar to enterocolostomy with exclusion, but is equally present in cases in which intestinal resection has been performed. This possibility is a real one. It can be avoided by taking pains either to carry the line of anastomosis almost up to the blind end or by performing an end-to-side implantation of the ileum into the colon. In the present series, we have encountered what we take to be two instances with such dilated blind ends, which could be demonstrated clinically, in one case, by the palpation of a large sausage-shaped mass, and in the other, by roentgenographic evidence. In a third instance, the formation of tension ulcers in the blind loop produced symptoms of peritonitis which required surgical intervention. This patient had been operated upon about two years previously, at which time an ileosigmoidostomy with exclusion had been performed for a hypertrophic colitis involving the transverse colon. The patient improved markedly following the operation and had practically no gastro-intestinal complaints. Twenty-four hours before readmission, he complained of sudden severe lower abdominal cramps, and vomited. Physical examination revealed temperature of 101° F, marked direct tenderness and rigidity in the right lower quadrant, and rebound tenderness throughout the lower abdomen. There was a moderate leukocytosis and the general picture was one of an acute appendicitis. Immediate exploration revealed the presence of a moderate quantity of seropurulent,

nonodorous fluid in the lower abdomen and pelvis. The appendix was normal. The cecum, ascending colon and terminal ileum were atrophic. Further exploration revealed that the blind loop of the ileum which had been used in the enterocolostomy was distended to about twice its normal size. The blind loop was about three inches in length and showed two areas about the size of a dime which were covered by exudate. Palpation revealed that these areas were markedly thinned. Resection of the blind loop was performed at a point about three-quarters of an inch distal to the stoma. The opening was then closed in layers. The pathologic report was "dilated ileum with two tension ulcers." The patient made an uneventful recovery and has remained well to date.

A third possible objection which has been voiced, especially in cases of ileosigmoidostomy, is that emptying of the fluid contents of the ileum into the sigmoid would result in diarrhea and might even prove irritative to the lower sigmoid and rectum. Such a diarrhea has not been observed in any case in which the sigmoid was found to be normal at the time of operation. As a matter of fact, in the right-sided colitis and ileitis the diarrhea which was previously present has disappeared. In a number of instances previously discharging perianal fistulae, instead of becoming aggravated, healed. There has been no impairment of control or development of any proctologic symptoms.

Fourth, the most frequent objection encountered has been that in the presence of such a long, blind, excluded loop of colon, stasis, retention, distention and ulceration might result in the segment of colon lying between the ileocecal region and the site of anastomosis. Here, again, clinical, radiologic and operative observations have brought no evidence which would tend to confirm such a belief.

The altered morphologic and physiologic conditions which resulted from ileocolostomy with exclusion have been carefully studied. The physiologic alterations were noted by careful, repeated inquiry into the nature of the patient's gastro-intestinal symptoms and activities. Thirty-two patients, 22 of whom have been followed for more than three years, were subjected to personal interviews and examinations. Results of this investigation may be summarized by saying that intestinal function following any of the above mentioned operations did not vary greatly from normal. The patients' appetites were good. Most of them had gained weight, some of them enormously so. With few exceptions they reported that after a few weeks they were having a maximum of three stools per day, and some were having only two movements, which were more or less normal in consistency, usually being described as "mushy" or "soft." They were neither diarrheal nor scybalous. Abdominal cramps were absent and defecation was as a rule unaccompanied by any dyschesia. Control was normal and when the desire to defecate overtook them at an inopportune time the desire passed away following inhibition. Most of these patients have only very rarely to resort to either cathartics or enemata. The only constant abnormal symptom complained of by these

patients, in approximately more than half the cases, was borborygmus and rumbling in the abdomen. This varied from a relatively minor symptom to a point where it became embarrassing in public. Another variation, which is perhaps worthy of note, was that dietary indiscretions were more apt to be followed by diarrhea. Incidentally, we may state that no attempt has been made to keep these patients on any specific diet. They have more or less eaten what they liked. In two instances symptoms were definitely traced to overeating of unusually large quantities of fruit or vegetables which produced frequent but not distressing bowel movements, in one case, and flatulence in another. It probably would be better policy to limit types of food tending to produce fermentation in the colon, and this, perhaps, might reduce the tendency toward excessive flatulence.

It is the authors' belief that a relatively small blind loop on the ileal side distal to the anastomosis is much more apt to show signs of dilatation and ulceration than is the unilateral excluded colon. This is probably due to the fact that retrograde peristalsis is present in the colon as a physiologic function, and that when an impulse is received distally, the colon can respond by emptying itself in the normal direction.

In order to visualize the mechanics of bowel function and to study morphologic changes which might be present, roentgenologic studies following a barium meal were made in 22 cases. By giving a barium meal it was possible to trace the course normally taken by the intestinal contents. These studies revealed that following ingestion of barium the medium commenced to reach the stoma within four to six hours. It was found that the ileal loop directly proximal to the anastomosis or immediately adjacent to it was dilated in almost one-third of the cases. Except in two cases, this dilatation was not accompanied by any tendency to stasis, and may be a manifestation of physiologic accommodation. In two instances, however, definite evidence of gas accumulation and retention of barium in the loop of ileum could be determined. In one of these cases, there had been an unusual dilatation of ileum noted from the onset of the patient's illness. This was a female, age 26, who was admitted to the hospital with acute, complete intestinal obstruction of about three days' duration. Study revealed that this was due to an obstructing lesion at the hepatic flexure for which a cecostomy was performed. At this time, enormous dilatation of the terminal ileum was noted. Three weeks later, an ileosigmoidostomy with exclusion was performed. In spite of the free drainage in the interim the marked distention of the ileum had not abated. At the final resection, a few weeks later, the continued dilatation of the ileum was again noted. In this instance, the distention of the ileum has apparently never returned to normal. The mechanism in the other case with this type of ileal stasis does not appear clear. All that can be said is that it was not giving rise to any clinical symptoms.

After passing the ileocolic stoma the barium stream was seen to pass both ways, part of it passed distally with normal peristalsis, and another portion, usually about equal in amount, was carried up the excluded proximal

colonic segment by retrograde peristalsis. The level to which retrogression occurred was determined by the site of the inflammatory lesion. In cases of inflammatory disease in the transverse colon, the barium was usually carried back to the region of the splenic flexure. In lesions in the right colon it passed, as a rule, to the level of the proximal transverse colon. In some cases of ileitis it was carried back as far as the cecum. The stream which passed distally was not expelled immediately. At the 12- and 24-hour observations it was found that most of the distal barium had been expelled. Some of the barium which had passed into the blind colonic loop by reverse peristalsis remained from 48 to 72 hours. Preliminary plates of the abdomen showed no marked gaseous distention in the excluded loop of colon. It is interesting to note that after the barium had passed into the colon there was never any demonstrable retrograde passage into the terminal ileum.

In a number of instances studies were made following a barium enema. Both the barium meals and barium enemata showed no abnormal dilatation or distention of the excluded colon, and haustrations and sacculations were normal, even after years of unilateral exclusion. When a barium enema is administered there is, as a rule, retrograde passage through the ileocolic stoma as well as into the excluded loop of bowel. Furthermore, the force of the barium enema is sufficient to carry the contrast medium to a point much farther proximal to the diseased segment than ordinary retrograde peristalsis. The only instance in which barium was trapped and became scybalous, was the result of such retrograde passage in the case of hypertrophic colitis.

Further opportunity of studying the physiology of the excluded colonic loop following ileocolostomy was afforded by two cases with fecal fistulae. In one of these, extensive obstructive resection had been performed for a carcinoma of the transverse colon in a very obese woman. An attempt to close the resultant artificial anus extraperitoneally was only partially successful, a small opening in the bowel remaining. An ileosigmoidostomy with exclusion was then performed to short-circuit the intestinal contents. This patient was examined on a number of occasions. It was found that the stool which could be observed in her transverse colon was solid. In another patient, an ileotransverse colostomy was performed for a large, prolapsing cecal fistula. Although there was considerable diminution of fecal drainage, a certain quantity of semisolid stool would appear at the cecal opening. Both these cases demonstrate that retrograde peristalsis with the functioning of the absorptive power of the colon takes place.

From a comparison of the bowel function following ileotransverse colostomy and ileosigmoidostomy with exclusion, no definite differences could be elicited. In summary, therefore, it would appear that the contents of the small intestine upon entering the colon at once pass in a retrograde direction to a certain extent. Whether there is any further retrograde extension of the material which originally passes into the distal loop cannot be stated. In any event, there is sufficient retrograde extension to permit of the normal absorptive functions of the colon to occur, and to render the stool solid or

semisolid The occurrence and extent of this retrograde peristalsis is important to bear in mind if a short-circuiting procedure is performed for a type of regional colitis affecting the splenic flexure and descending colon In such instances, ileosigmoidostomy alone is probably insufficient to protect the diseased bowel from the intestinal contents In this type of case, division of the colon just proximal to the anastomosis must be performed as recommended by Berg³ and von Beck⁴ Further evidence that there is no unusual dilatation or stasis in the excluded loop of colon was obtained in five instances by secondary operation, all following a period of at least a year, and, in two cases, for periods of more than five years No abnormal dilatation, distention, thickening, or atrophy of the excluded loop could be appreciated

The question may arise as to why ileosigmoidostomy rather than ileotransverse colostomy was performed in such a large percentage of cases In the first place, it seemed logical to assume that because of the tendency to retrograde peristalsis, much better exclusion of the diseased segment of bowel could be obtained Second, in carcinomata, especially near the hepatic flexure, it was felt that if necessary, more radical resection because of lymphatic node involvement could be carried out, and if necessary the main branch of the middle colic artery could be divided Third, experience has shown that in cases of right-sided hypertrophic colitis it might not be possible to absolutely ascertain that the anastomosis was being performed in a healthy segment of transverse colon Fourth, in cases in which fistulae were present it seemed obvious that less opportunity for leakage of intestinal contents would occur, the more distally the ileocolic anastomosis was placed Fifth, the lateral anastomosis appeared to be technically safer and simpler to perform in the more muscular sigmoid than it was in the transverse colon with its sacculations and haustrations

In regional ileitis, however, experience with recurrences proximal to the line of anastomosis has led us into more frequently performing ileotransverse colostomy In such cases a secondary exclusion operation can be performed by dividing the ileum proximal to the diseased area and then anastomosing the bowel with the sigmoid

It is our opinion that the physiologic alterations produced by ileocolostomy with exclusion are not sufficient to give rise to any pathologic symptoms, with the exception of possible distention and ulceration caused by leaving too long a segment of small intestine beyond the area of anastomosis Occurrence of intestinal symptoms, such as abdominal cramps and persistent diarrhea, has, in our experience, been due to a recurrence or extension of disease in the bowel In instances in which the primary operation has been undertaken for lesions in the ileum, the symptoms have been found to be due to recurrence of the disease in the ileum proximal to the site of anastomosis In cases of primary colonic disease, recurrence of symptoms has usually been due to persistence of the disease or extension to a more distal segment of colon This possibility has been avoided by limiting this type of operation to the definitely localized granulomatous, hypertrophic types of colitis

In this regard, it is of interest to cite a case operated upon on the service of Dr. Richard Lewisohn and previously reported by him.² In this patient, ileotransverse colostomy with exclusion was performed for an extensive terminal ileitis. For a few months the patient was considerably relieved but recurrence of diarrhea forced her readmission. At this time, the previously excluded loop of ileum as well as cecum were resected. They showed marked regression in the pathologic findings. For a while the patient's symptoms again subsided but episodes of abdominal pain and diarrhea again recurred. Roentgenologic examination at this time revealed a lesion in the small bowel just proximal to the stoma, which was again resected and an ileosigmoidostomy was performed. Since that time, this patient has again had recurrence of symptoms and again a lesion proximal to the anastomosis has been discovered roentgenologically. It is interesting to note that at the time of the resections, in neither instance did the excluded loop of bowel show any marked changes.

One drawback to ileosigmoidostomy and subsequent resection, as above described, occurs in cases of malignant disease, because either a recurrence or development of a new tumor in the blind loop of bowel will, at first, be practically symptomless. In one such instance, the only symptom of a neoplasm, that occurred in the blind loop, was a rapidly developing anemia. In this patient, an ileosigmoidostomy had been followed by a wide resection of bowel, carried from the terminal ileum to the transverse colon for a double carcinoma of cecum and hepatic flexure. The patient was seen about one year later with a history of weakness and anemia. The stool was strongly positive for blood. Barium enema showed a filling defect in the transverse colon where a new tumor had apparently developed. However, if careful track is kept of the patients with malignant disease and an early diagnosis is made, further resection in these cases of multiple carcinomata is simpler than if an ileotransverse colostomy is present.

There are certain technical features which may perhaps be emphasized. In the first place, it has become our custom to perform the ileocolostomy through a left-sided incision. We found that this permits an adequate exploration and exposure of the ileocecal junction. The advantage of the left-sided incision is that secondary procedures on the right colon are rendered much more simple, technically, as massive adhesions sometimes develop in the operative field. Furthermore, there is a certain sense of security, and undoubtedly more healing power, resulting from a fresh wound than that following the reopening of an old one. Also, if infection of the wound should occur when the left rectus incision is used, the second stage will not be held up too long. Infection of a right-sided wound might delay such a secondary resection for a considerable length of time.

We cannot emphasize too strongly the necessity of visualizing the ileocecal junction and being positive that it is the proximal portion of the divided bowel which is being anastomosed. We know of instances in which the distal loop has inadvertently been the seat of the anastomosis. Another difficulty which deserves mention and which can be circumvented by proper technic, is

the occurrence of adhesions of the blind loops to each other or to the stoma. To avoid this, we have at times excised a small segment of ileum and inverted the distal closed end into the distal ileum to a greater extent than usual. However, we have found that if division of the mesentery is carried far enough down, the necessary independent mobility will usually be achieved. Incidentally, it is our belief that too long a blind loop is much more apt to be left behind, distal to the ileocolic anastomosis, if division is practiced at the second stage rather than the first. In such cases one hesitates to approach too closely to the relatively fresh stoma, and the frequent presence of inflammatory induration in the immediate vicinity of the anastomosis also tends to lead the operator to divide the ileum more distally.

SUMMARY AND CONCLUSIONS

A group of 32 cases of ileocolostomy with exclusion are reported. Clinical, roentgenologic, and operative studies in this series revealed

(1) That obstruction and dilatation of the distal excluded ileum did not occur.

(2) That in the case of ileosigmoidostomy there was no irritative effect on the lower bowel.

(3) That, although there was retrograde passage of ileal contents into the excluded segment of colon, there was no abnormal distention, dilatation or ulceration of this loop.

(4) The only site at which definite pathologic alterations occurred as a result of the operative procedure, was in the blind end of terminal ileum used in a side-to-side anastomosis. In two cases, there was marked distention of this blind end and in one case tension ulcers produced peritonitic signs necessitating resection of the blind loop.

(5) The operation of ileotransverse colostomy or ileosigmoidostomy with exclusion does not in itself produce symptoms. Recurrence of symptoms has been found due to recurrence of the disease proximal to the anastomosis when the original operation was undertaken for disease of the small intestine. In cases in which the operation was performed for the localized type of colitis, symptoms have been found to be due to either persistence of the disease in the excluded loop of colon or its extension distally.

(6) In view of the fact that ileocolostomy with exclusion does not produce any untoward gastro-intestinal symptoms, it might be advisable to use this procedure as a first-stage operation for inflammatory diseases of the right colon and terminal ileum. The necessity for further intervention could then be judged by the future course of the disease.

REFERENCES

- ¹ Estes, W. L., Jr., and Holm, C. E. *ANNALS OF SURGERY*, 96, 924, November, 1932.
- ² Lewisohn, R. *Surg, Gynec, and Obstet*, 66, 215, February, 1938.
- ³ Berg, A. A. *ANNALS OF SURGERY*, 104, 1019, December, 1936.
- ⁴ von Beck, Bernhard. *Beitr. z. klin. Sch. Chir.*, 84, 339-343, 1913.

DISCUSSION —DR JOHN DEJ PEMBERTON (Rochester, Minn.) I would like to discuss very briefly one or two points regarding ileitis. In December, 1936, I reported all the cases of regional enteritis seen at the Mayo Clinic in the 15-year period 1922 to 1936, inclusive. There were 39 cases, and at that time I attributed the increased incidence in recent years to an increased alertness on the part of the clinician and the roentgenologist in recognizing the disease. However, in the past 30 months we have seen 68 cases, that is, there have been almost twice as many cases in the last three years as in the prior 15 years. I now feel, very definitely, that the disease is on the increase.

Because of this fact and because we know very little, or nothing, regarding the cause, I think it is exceedingly important that this subject be repeatedly brought to the attention of the profession.

Our experience has led us to believe that the best treatment for regional ileitis is the resection of the affected segment or segments involved, either in a one-stage or two-stage procedure, depending upon the conditions found in the individual case. When a two-stage procedure is employed because of the presence of a fistula or of the poor general condition of the patient, I believe that a period of two to six months should elapse between the stages. This allows, of course, for the rehabilitation of the patient as well as for a partial resolution of the inflammatory process. I do not believe that the period should be longer than six months, because of the risk of extension of the inflammatory process.

In many of our cases, because of marked improvement obtained following ileocolostomy or a short-circuiting procedure, we have delayed the second operation for several years, in some this has been delayed as long as five years. In none of these cases have we seen complete resolution, but on the contrary, in several of the cases we have seen definite extension of the process to involve the ileum at the site of anastomosis or proximal to the site of the anastomosis.

There is another reason why I think it is important to resect the infected part of the ileum, this is because the process sometimes is tuberculous, and yet it is indistinguishable grossly from the nontuberculous type of ileitis. I recently operated upon a patient, upon whom I had performed an ileocolostomy six months before, for what was thought to be nontuberculous enteritis, but the pathologist found that the lesion was tuberculous.

TABLE I

CASES OF REGIONAL ENTERITIS IN WHICH OPERATION WAS PERFORMED FROM
JANUARY 1, 1922, TO APRIL 30, 1939, INCLUSIVE

No. of Cases	Surgical Procedure	Hospital Deaths	Mortality, Per Cent
6	Abdominal exploration*	1	16.7
30	Exclusion or short-circuiting operation	6	20.0
32	One-stage resection and anastomosis	2	6.3
39	Two-stage anastomosis and resection	1	2.6
<hr/>		<hr/>	<hr/>
Total 107		10	9.3

* One case, enterostomy, one case, drained and closed fistula.

Table I shows the cases of regional enteritis seen in the clinic from January 1, 1922, to April 30, 1939, inclusive, of which we have definite record. Parenthetically, cases of lesions of the small bowel seen prior to 1922 have not been reviewed. The cases listed under abdominal exploration were, for

the most part, cases in which the lesion was very extensive and in which no major surgical procedure was performed. The mortality rate in the exclusion operation was high, not because the operation in itself was more hazardous than the operation of resection but because of the very poor condition of the patients. There were two deaths in the group of 32 cases in which resection was carried out in one stage. The group was comprised, of course, of selected cases. I think it is particularly interesting that of the 39 cases in which resection was carried out in two stages there was only one death. It seems to me, therefore, that, if the patient can endure a preliminary ileocolostomy, resection of the affected segment of bowel should be performed later, since resection can be accomplished at small risk.

DR VERNON C. DAVID (Chicago, Ill.) The essayists have discussed the subject of ileocolostomy with thoroughness, and have raised a number of interesting technical and physiologic problems for discussion.

As to the indications for ileotransverse colon colostomy, I would hazard the opinion that they are much the same in all clinics. During the last three years at the Presbyterian Hospital, Chicago, the operation was carried out 27 times (Table I).

TABLE I

Carcinoma of the cecum and ascending colon	10
Carcinoma of the hepatic flexure	2
Carcinoma of the ileocecal valve	1
Lymphosarcoma of the cecum	3
Postoperative obstruction after appendicitis	2
Granuloma of the cecum	1
Intractable fistula of the cecum	1
Terminal ileitis	7
	—
Total	27

There were five deaths in this group, all of whom had a tumor, one from embolism and four from peritonitis, three of these deaths occurred in inoperable cases where the operation was performed to relieve obstruction.

The title "Ileocolostomy with Exclusion" raises the question as to whether an ileocolostomy should always be performed after division of the ileum as the authors indicate. We practically always perform the operation without division of the ileum when the operation is undertaken to relieve obstruction or purely as a side-tracking procedure, and have had reason to believe that the new and wide lateral anastomosis between the ileum and transverse colon actually did side-track the fecal stream. I would like to cite one informative case.

A large cecal fistula, following accidental injury during a nephrectomy, persisted in spite of repeated efforts at closure. An ileocolostomy in continuity produced a dry and practically feces-free field which allowed prompt healing of the fistula after operation. The efficacy of the operation in terminal ileitis is more difficult to estimate due to the tendency for the disease to have multiple and often recurrent lesions, developing months or years apart. We believe with the essayists that a side-tracking operation as the first-step procedure in terminal ileitis, especially if a fistula is present, is a sound procedure.

The question of a one- or two-stage operation in carcinoma of the cecum, ascending colon, or hepatic flexure, must be left to the individual operator's judgment, all agreeing that obstruction, adiposity, poor cardiovascular quotient, or marked local inflammatory reaction about the tumor should call for

a preliminary ileocolostomy. Wherever possible, however, we believe in the one-stage operation with a wide lateral anastomosis between the ileum and transverse colon in preference to the end-to-side aseptic method.

I should like to call attention to the possibility of a carcinomatous implant at the site of the anastomosis in a two-stage operation. That implants take place, is rather dramatically evidenced in a patient who had had an extensive horseshoe rectal fistula for five years, upon whom several operations had been performed and several biopsies made, all showing chronic inflammatory tissue. At the last operation, the lining of the fistulous tract was friable and a biopsy showed it to be a papillary adenocarcinoma. On questioning the patient, he admitted having had rectal bleeding for three months. Proctoscopic examination showed a small papillary carcinoma 15 cm above the anus. We have had another patient who developed a small carcinoma at the junction of the skin and the mucosa of a colostomy performed as a preliminary first-stage operation for carcinoma of the rectum. While implantation of carcinoma at the site of an ileocolostomy is undoubtedly rare in the two-stage operation, it must be considered as a relative indication for the one-stage procedure.

The essayists' remarks on ileosigmoidostomy were very interesting to me, in that they have observed no tendency for the patient to have liquid stools resulting from retrograde passage of the fluid contents of the ileum into the ascending and transverse colon. I have avoided the operation wherever possible because of the supposed tendency to diarrhea, and would still be inclined to employ an ileotransverse colon anastomosis wherever possible, as it physiologically places the liquid contents of the small loop as far to the right in the colon as possible and excludes the dangers of a large blind loop.

DR RALPH COLP (closing). There is very little that I can add except to reiterate that the cases in which an ileosigmoidostomy with exclusion has been performed have not complained of diarrhea after the first few weeks, and if they did complain of diarrhea at a subsequent period, it could be taken for granted that there was some extension of the disease.

THE VALUE OF PRELIMINARY COLOSTOMY IN THE CORRECTION OF GASTROJEJUNOCOLIC FISTULA*

DAMON B PFEIFFER, M D

PHILADELPHIA, PA

ASSISTED BY

EDWARD M KENT, M D

NORWICH, CONN

FROM THE PFEIFFER SURGICAL CLINIC OF THE ABINGTON MEMORIAL HOSPITAL, ABINGTON, PA

OVER THE YEARS there have appeared in the literature instances of spontaneous fistulous communications between stomach, duodenum, jejunum and colon in varying combinations, produced by a variety of lesions such as gastric or colonic carcinoma, abdominal tuberculosis or pyogenic abscess, ulcerative colitis, trauma and unoperated ulcer of the stomach or duodenum, the last such case being reported by Wilkie¹ However, following the employment of gastro-enterostomy for ulcer in cases which we now know were unsuitable, the formation of a gastrojejunal or jejunal ulcer was not infrequent, and in a number of cases, by adhesion and continued erosive action, a communication was made between the stomach, jejunum and colon—the gastrojejuno-colic fistula

Just as the etiology of peptic ulcer is not definitely known, so the cause of these new ulcers at or just beyond the stoma is not understood or controllable The first such ulcer was reported by Braun,² in 1899 The frequency of occurrence varies widely in different statistics Lahey³ found the discrepancy to range from 17 to 24 per cent after gastro-enterostomy, and from 0.4 to 10 per cent after gastric resection Lahey and Swinton⁵ recommend two technical points which are probably of value in prevention, namely, the avoidance of entero-enterostomy and of occlusion of the pylorus But it is evident that the problem is not one of technic alone It is agreed that gastro-enterostomy in the young, sthenic, hyperkinetic, hyperacid type of individual is unwise because of the danger of subsequent ulcer occurring at the stoma

In order to prevent the still more serious state which ensues when the ulcer perforates into the colon, it is recommended by some to make an anterior gastro-enterostomy, or if a posterior gastro-enterostomy is made, to place the opening in the transverse mesocolon near the base rather than near the colon

Czeiny, in 1903, reported the first case of gastrojejuno-colic fistula following gastro-enterostomy Since then, a considerable number of cases have been reported in the literature, either as isolated case reports or in small series They may occur within the first year after gastro-enterostomy or only after many years have elapsed They may be small or large and may be direct or through the medium of a fistulous tract, usually short The symptomatology and diagnostic signs have been constructed These consist of (1)

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

Pain, not necessarily of ulcer character, and as in primary ulcer, inconstant and sometimes inconspicuous or absent, (2) diarrhea, with symptoms simulating colitis resistant to medication and diet, and the passage of undigested food recently taken by mouth. This has been thought to be due to direct passage of food from stomach or jejunum into the colon but we believe, on the basis of fluoroscopic findings, that it results from the exceedingly rapid transport of food through the stomach and intestines and is probably due to the irritation of the tract from the presence of colonic contents in the stomach and bowel (ref roentgenologic examination of Case 2), (3) eructation of foul gases and vomiting of material obviously resembling colonic contents often occur, (4) general responses are loss of weight and strength, frequently extreme, with anemia and blood protein disturbances.

Such symptoms, when seen in characteristic form, make the diagnosis extremely probable. Roentgenologic examination is always advisable in doubtful cases and for verification in all cases. Deformities, extreme hyperperistalsis extending throughout the small intestine, the visualization of the fistulous tract or the actual passage of opaque mixture from colon to stomach or vice versa, are the suggestive or positive signs.

The treatment of anastomotic ulcer by medical management is not so successful as is that of primary gastric or duodenal ulcer, and the results are more difficult to check. Unless a satisfactory measure of success is obviously forthcoming, it would seem wiser to reoperate upon these cases and carry out an extensive gastric resection. When fistula has once formed, it might almost be said that there is no medical treatment. It has been the general experience that diet, alkalis and other adjuncts have little or no favorable influence upon a fistula once established. Delay results only in further deterioration of the patient as a surgical risk confronting an operation which is necessarily formidable.

The prognosis without operation is exceedingly grave. In most cases there is progressive inanition and early death from perforation, hemorrhage or intercurrent disease. On the other hand, operation has, hitherto, proved to involve great hazard. Loewy¹³ discusses a collected group of 63 cases which were corrected surgically with a mortality of 27 per cent. Verbrugge⁶ describes a group of 20 cases with operative mortality of 25 per cent. Allen¹¹ reports two deaths in eight cases (25 per cent). Lahey lost five out of eight patients, mortality 63 per cent, albeit but one died of peritonitis. On his recent visit to this country, Finsterer recounted his personal operative experience with one-stage gastrojejunal resection, which yielded five deaths in 13 cases (38.4 per cent). He quoted Gosset as having collected 28 cases with 12 deaths (42.8 per cent). From my personal knowledge of such cases operated upon and never reported, it seems probable that the total mortality is much higher than these figures. Personally, prior to adoption of the procedure herein advocated my own experience, fortunately, comprised only two cases. Both died following one-stage operations, though the technical procedures were satisfactory and not attended by shock, hemorrhage or gross contamination. One died of peritonitis, the other of bronchopneumonia which he was unable

to combat, though he lived four weeks after operation. Both were in bad general condition, having grown progressively worse over a long period of attempts at improvement under medical management. It seemed to me then, and it seems to me now, that any operation of magnitude performed upon subjects in such a low state of nutrition and resistance will inevitably be attended by a high percentage of complications and mortality.

It was with such a background that I encountered the following case in the Abington Memorial Hospital.

Case 1—K. E., white, male, age 34, was seen first, September 14, 1936, complaining of severe diarrhea, voracious appetite, marked weakness and fatigue, and loss of 30 pounds. A gastro-enterostomy had been performed elsewhere four years previously, following which, he had been improved until the onset of his present symptoms, five months before.

Physical Examination revealed a pallid, emaciated man, with boggy, slightly distended abdomen and moderate tenderness in the epigastrium. On auscultation peristalsis was in a continual state of unrest. Slight pitting edema of the ankles was observed. There was a moderate hypochromic anemia. The urine was normal. Fractional gastric examination revealed a Grade 4 hyperacidity. Sigmoidoscopic examination was unsatisfactory due to a constant trickle of liquid, frothy feces containing mucus and particles of partially digested food. The mucosa was intensely congested but not ulcerated.

Röntgenologic Examination—The barium passed out of the stomach too rapidly to permit of adequate study. Some went through the pylorus but the bulk left by way of the stoma. The stomach was completely empty in 15 minutes. All was passed along through the small intestine with great rapidity. No barium could be seen passing directly into the colon from the stomach. By barium enema this mixture was seen fluoroscopically to freely enter the proximal third of the stomach, directly from the distal part of the transverse colon, giving definite evidence of gastrojejunal fistula.

He was placed on ulcer regimen and sent home, but returned in two weeks with symptoms uninfluenced, and was given two transfusions in preparation for operation.

First Operation—October 2, 1936. Considerable excess of clear peritoneal fluid was present. The scar of a healed anterior duodenal ulcer was noted. At the site of the gastro-enterostomy, the stomach, colon and jejunum were matted together and surrounded by adherent mesenteric structures and omentum, the whole forming a mass almost as large as a fist. Still more striking was the highly inflammatory state of the tissues. The adjacent gastric wall was edematous. The proximal and distal loops of the jejunum were greatly thickened and congested and showed shaggy exudate from the serous surface and actual small plaques of new fibrin. In addition to the fistula, there were two jejunal ulcers, one 2 cm., the other 8 cm., below the anastomosis. It was obvious that radical surgery could not be safely performed upon such tissues. Recalling that this fistula apparently worked in only one direction, that is, from colon to stomach, it occurred to me that preliminary colostomy might favorably influence the conditions present. Accordingly, a loop of ascending colon was brought out through a muscle splitting incision external to the semilunar line. The loop was opened on the third day and function promptly established. Recovery was uneventful. All symptoms disappeared. Nineteen days after operation, he was discharged with no digestive trouble, excellent appetite and gain in weight. He was having no movement by normal channels.

Three months later, January 25, 1937, he was readmitted for operation, having gained almost 50 pounds, feeling and looking well. He had had no evacuations by rectum. Roentgenologic reexamination showed barium leaving by way of the gastro-enterostomy into the jejunum but none into the colon. On barium enema, however, barium could be seen entering the stomach directly at the old site.

Second Operation—February 1, 1937. The abdomen was reopened through the for-

mer left paramedian incision. The change in condition was truly unexpected and astounding. There was no excess peritoneal fluid. The inflammatory mass was smaller, the walls of both stomach and jejunum, in relation to the anastomosis, were normal in thickness and consistency and were uninfamed. Since the old duodenal ulcer was apparently healed and the pylorus patulous, it was decided to take down the anastomosis and make the necessary repairs to restore the normal anatomy. The stomach was disconnected and closed. The jejunum and colon were detached and repaired. Curiously enough, at this time there was no more ulceration at the site of the fistulous communication. The jejunal ulcers also had disappeared. The operation was somewhat extensive and time-consuming but was carried out upon good tissues and without danger of contamination from the colon.

Recovery was without incident except for extensive distention on the third day, for which a simple purse-string jejunostomy was performed under local anesthesia. On the tenth day, crushing of the spur of the colostomy was begun and completed six days later. The colostomy was closed (third-stage Mikulicz), March 9, 1937. Healing was prompt and no digestive symptoms remained.

Roentgenologic examination, March 22, 1937, showed irregularity of mucosal pattern of stomach, nonfilling duodenal cap, empty at three hours. Barium enema showed a normal somewhat hypotonic colon. Gastric analysis still showed hyperacidity, maximal in one hour, total 95, free acid 75. He was placed on ulcer regimen, returned home, and has remained well, pursuing his usual occupation as shoemaker.

Struck by these findings and the alteration in conceptions of the pathologic physiology thus suggested, and the possibility of lowering the high mortality of surgical treatment which seemed to be presented, another case was anxiously awaited.

Case 2—R. B., white, male, age 29, was admitted to the Abington Memorial Hospital, June 3, 1938, complaining of diarrhea, fecal vomiting and belching of gas with fecal odor, diffuse abdominal pain and loss of more than ten pounds, all occurring within the preceding five weeks. He had had an appendectomy in May 1927. In August, 1929, a perforated duodenal ulcer was closed by simple suture. In February, 1937, a recurrence of duodenal perforation occurred and this time, in addition to closure of the perforation, a posterior gastro-enterostomy was performed. All these operations were performed by other surgeons. About five weeks following the closure of perforation and performance of a gastro-enterostomy, the patient began to complain of pain in the left lumbar region which persisted for six months and then subsided for eight months. About two months before present admission, the pain recurred in the left lumbar region but was most severe somewhat higher than previously. This pain was relieved temporarily by alkalies and food, and persisted for about one month, to culminate in the symptoms presented when seen in June, 1938.

Physical Examination revealed a pallid, undernourished male adult. Peristalsis was alternately ferocious and inaudible, abdominal tenderness was rather general in the upper quadrants but was most marked over a small area just below and immediately to the right of the umbilicus. Urinalysis, complete blood chemistry, blood Wassermann and Kahn were all negative. Blood counts revealed moderate secondary anemia. Barium administered orally was seen to leave the stomach through both pylorus and gastro-enterostomy, but easy flow of radiopaque medium was seen by way of a fistulous communication of the jejunum with the colon. Barium enema even more clearly revealed this communication through which radiopaque material passed easily from a point just proximal to the splenic flexure of the colon directly into the stomach and jejunum. Two preoperative blood transfusions were administered.

First Operation—June 8, 1938. Under spinal anesthesia, celiotomy disclosed numerous adhesions of the omentum both to viscera and parietes. The posterior gastro-enteros-

tomy could be visualized and the ascending arm of the transverse colon was found firmly attached to the anastomosis. The jejunum, both above and below the anastomosis, was seen to be dilated, thickened, reddened and edematous. This inflammatory process extended in some measure to the mesentery and to the attached colon. The ascending colon was mobilized and a loop colostomy was made through a stab wound in the flank. This loop of bowel was opened with the cautery five days later, and postoperative convalescence was uneventful. Three weeks postoperative, he was discharged to the care of the Gastro-Enterologic Clinic of the hospital. However, two days before discharge, the continued existence of the fistula was verified roentgenologically.

Four months after colostomy had been performed, the patient was readmitted. He had had no digestive disturbances and had gained greatly in weight. In the interval, there had been absolutely no diarrhea but there had been normal stools from the colostomy and some by rectum. The continued presence of the fistula was again verified roentgenologically. All evidence of secondary anemia had disappeared.

Second Operation—Under spinal anesthesia, the site of the old gastro-enterostomy was exposed. The pylorus was patulous and the duodenal ulceration had apparently healed. The inflammatory changes in the jejunum and surrounding viscera noted at the previous operation were entirely absent. A jejunocolic fistula, measuring 3.1 cm., was found. The jejunum was dissected free and the opening in its wall closed. The defects in the colon and stomach were similarly closed, thus reestablishing normal continuity. A Stamm jejunostomy was performed just distal to the repaired area. The postoperative course was uneventful. The spur was destroyed and the colostomy opening repaired three and one-half weeks later, and the patient was discharged, five weeks after correction of the fistula.

He is continuing his ulcer prophylaxis regimen. Unfortunately his duodenal ulceration has become reactivated, and he has been urged to have a gastric resection performed, since he seems to fall into the group in which no operation short of this will prevent recurring peptic ulcer. Perhaps it would have been better judgment in view of this patient's history, to have done this instead of restoring normal continuity. In our opinion, it would have been feasible under the conditions present after preliminary colostomy but not before.

In February, 1938, I briefly reported the first case before the Joint Meeting of the New York Surgical Society and the Philadelphia Academy of Surgery. Shortly after this, Dr. Ralph Colp, of New York, adopted the suggestion and met with an even more striking evidence of the favorable influence of preliminary colostomy. He has been kind enough to furnish me with his notes on this case and to authorize me to use them here, for which I make grateful acknowledgment.

Case Report—Dr. Ralph Colp. A male, age 49, was admitted to Doctor Colp's service January 7, 1935, and discharged January 24, 1935. He gave a nine-year history of ulcer type. Roentgenologic examination verified the presence of a penetrating duodenal ulcer with a large residue remaining after five hours. A retrocolic, posterior no-loop gastro-enterostomy was performed, followed by uneventful recovery and cessation of symptoms for three years. Three months before his second admission, April 13, 1938, he began to have frequent bowel movements accompanied by the belching of fecal-smelling gas. He had lost ten pounds. Barium enema revealed the presence of a gastro-jejunocolic fistula. A colostomy of the Mikulicz type was made with the ascending colon through a muscle splitting, right rectus incision. When the colostomy was established on the sixth day, almost immediately the patient observed that his breath was no longer foul. He was discharged symptom-free. After three months and a gain of 18 pounds, he was readmitted, July 8, 1938. The former fistula could no longer be demon-

strated roentgenologically Barium in the stomach passed through the stoma into the jejunum but not into the colon Barium enema injected through the colostomy showed irregularity of the midportion of the transverse colon but did not pass into the stomach

Operation—July 16, 1938 A hard inflammatory mass, the size of a lemon, which included the stomach, colon and jejunum, was revealed About 12 inches from the duodenojejunal angle, the efferent jejunum seemed to be the seat of an ulceration The fistula in the colon had evidently healed The stomach was still much dilated A partial jejunectomy with end-to-end jejunojejunostomy and a subtotal gastrectomy with a Hofmeister antecolic gastro-enterostomy was performed The pathologic examination showed that the ulcer of the jejunum above noted had healed After moderate reaction, the patient did well Beginning two weeks later, the colostomy was repaired in the Mikulicz fashion In March, 1939, the patient was seen and found well He had gained 25 pounds

In commenting on these cases, it is important to note that it is generally believed that in most cases of gastrojejunocolic fistula there is a large loss of gastric contents into the colon, whereas actually in the first case there was no passage from stomach or jejunum into the colon but only in the reverse direction The second case, however, was demonstrated roentgenologically to possess free flow in both directions by way of the fistulous communication This was verified clinically, for colostomy resulted in no stool by rectum in the first patient, while in the second, stools were passed by rectum as well as through the artificial anus This is important, for it lends forceful evidence to our belief that the devastating diarrhea seen in these patients is due to the presence of colonic contents within the upper intestinal tract, and that this can be controlled by diversion of the large bowel fecal current at a point above the fistula

The choice of procedure is highly important in the surgical management of these patients It has been pointed out that simple restoration of continuity has more adherents than the more radical corrective measures We have no desire to enter into this question at this time, and we do not mean to imply that the use of restoration of continuity in these two instances indicates the nature of our preference in the matter We do wish, however, to emphasize our belief that preliminary colostomy is compatible with any surgical plan in these cases and that it will undoubtedly prove of even greater value in those cases selected for the more radical procedures

The effects produced by this procedure are apparently due to diversion of colonic contents from the stomach and small bowel When the contents of the colon are being continuously regurgitated into the stomach and jejunum, the patient is continuously fed upon *feces* It would seem that either by reinfection from the colon or by changes in gastric physiology, the anastomotic ulcer is continuously reactivated and that there is a definite tendency toward the formation of additional jejunal ulcers It is worth noting that in Case 2, in which the fistula worked both ways, the discharge from the stomach into the distal colon after colostomy did not cause diarrhea or colitis, and did not interfere with nutrition Small bowel movements occurred but in all essential respects the favorable effects of the preliminary colostomy were equal to those noted in Case 1, in which the fistula appeared to have a valve-like formation

which allowed only the colon contents to enter the stomach and not vice versa. Clinically, the observations noted following this procedure were cessation of diarrhea with return of the patient to excellent physical state and hence reduction of the general risks of surgical intervention. Furthermore, the inflammatory reaction of adjacent tissues and the jejunal ulceration entirely subsided, thus reducing the risk of inflammatory complications in surgical correction of the fistula. A third effect of preliminary colostomy is freedom from contamination at operation and the later protection of suture lines in the repaired colon, abolishing the danger from leakage at this point.

It seems advisable to incorporate jejunostomy in the operation when the fistula is corrected, and this has been noted previously by Findley,¹⁵ and Waters and Priestly.¹⁰

The use of cecostomy at the time of correction of the fistula has been reported by Bolton and Trotter,¹⁶ Balfour,¹⁷ and MacDonald,⁴ and was recommended as a measure to protect the suture lines in the repaired colon, especially when such repair has been difficult. Exteriorization of the colon by some modification of the Mikulicz procedure has likewise been employed (Mason and Baker,¹⁸ MacDonald,⁴ Pauchet,¹⁹ and Findley¹⁵). In their hands, the procedure was carried out at the time of the correction of the fistula and for the purpose of avoiding a suture repair of the colon with potential leakage and peritonitis. The single instance found in the literature in which either of the above procedures was employed as a preliminary measure to the correction of such a fistula was reported by Colucci,²⁰ and in this instance a cecostomy was performed upon a patient with symptoms suggesting intestinal obstruction. A gastrocolic fistula was later demonstrated and was apparently the result of spontaneous perforation of a gastric ulcer into the colon. No gastroenterostomy had been performed. Five months later, the fistula was corrected, and still later, the cecostomy closed. The same improvement in the patient's general condition and disappearance of clinical signs of intraperitoneal inflammatory reaction were noted by Colucci as were seen in the case we are reporting. This experience tends to strengthen the case for preliminary diversion of colonic contents from the upper gastro-intestinal tract. Who would doubt the superiority of loop colostomy over cecostomy in bringing this about? The question of the method to be employed in dealing with the ulcer problem presented at the second stage is beyond the scope of this paper. Recurrence of ulceration would seem to call for more radical procedures than simple repair and restoration of continuity. If so, preliminary colostomy offers a means of making the more complicated measures both simpler and safer.

CONCLUSIONS

(1) Loop colostomy preliminary to correction of gastrojejunocolic fistula resulted in cessation of symptoms and return of the patients to their normal physical state, thus greatly reducing the operative risk.

(2) Complete disappearance occurred of intraperitoneal inflammatory reaction involving the jejunum, colon, their mesenteries and the adjacent peritoneum. In two instances the ulcerations themselves disappeared.

(3) Colonic contamination was avoided and adequate protection of the repaired transverse colon was secured, thus abolishing the danger of leakage and peritonitis

(4) The disastrous general and local results of gastrojejunocolic fistula are in large part due to reflux from the colon into the upper digestive tract and not from loss of gastric contents into the colon, as hitherto suggested

(5) Preliminary colostomy is indicated before attempts to carry out the formidable procedures necessary to correct gastrojejunocolic fistula

BIBLIOGRAPHY

- ¹ Wilkie, D P D ANNALS OF SURGERY, 99, 401, 1934
- ² Braun Verhandl d deutsch Gesellsch f Chir, 28, Part 2, 94, 1899
- ³ Lahey, F H Am Jour Digest Dis and Nutrition, 2, 673, February, 1936
- ⁴ MacDonald, Ian Lancet, 2, 804, October 15, 1927
- ⁵ Lahey, F H, and Swinton, N W Surg, Gynec and Obstet, 61, 599, November, 1935
- ⁶ Verbrugge, J Arch Surg, 2, November, 1925
- ⁷ Monroe, R T, and Emery, E S Can Med Asso Jour, 18, 272, March, 1928
- ⁸ Gatewood Surg Clin North Amer, 2, 99, February, 1931
- ⁹ Katzoglu, P Deutsch Ztschr f Chir, 1, 221, 1929
- ¹⁰ Waters, J T, and Priestly, J T Proc Staff Meet Mayo Clin, 8, May, 1933
- ¹¹ Estes, W L, Jr ANNALS OF SURGERY, 96, 250, 1932
- ¹² Scrimger, F A C ANNALS OF SURGERY, 104, 594, 1936
- ¹³ Loewy, G Paris, Desfosses, 1921
- ¹⁴ Allen, A W Surgery, 1, 338 March, 1937
- ¹⁵ Findley, F M Arch Surg, 32, 896, May, 1936
- ¹⁶ Bolton, C, and Trotter, W Brit Med Jour, 1, 757, 1920
- ¹⁷ Balfour, D ANNALS OF SURGERY, 82, 421, September, 1925
- ¹⁸ Mason, J T, and Baker, J W Surg Clin North Amer, 11, 1097, October, 1931
- ¹⁹ Pauchet, V Prat Chir Illust Fasc, IX
- ²⁰ Colucci, C Policlinico (sez chir), 40, 439, August, 1938

DISCUSSION —DR FREDERICK A COLLER (Ann Arbor, Mich) Gastrojejunocolic fistulae are notoriously unsatisfactory to treat, and I am sure Doctor Pfeiffer has made a real contribution in the procedure that he has described this morning. As he stated, the operative mortality is high, patients may die from shock because the operation is a prolonged one, on undernourished patients. Postoperative pulmonary complications are common, and of course peritonitis is an ever present danger, and a very frequent complication and cause of death, because one is working with three organs that contain colonic contents.

Two years ago, Dr Arthur Allen advised and described a method for aseptic resection of this lesion, and I have employed it with satisfaction in the smaller lesions. However, I have found that I, at least, cannot use it in some of the larger lesions such as those described by Doctor Pfeiffer and I believe that his procedure has a real place as a preliminary to the aseptic method which can be employed at a later date.

There is another factor, however, that I think one should stress here. You cannot find a patient with a higher degree of malnutrition than these people present. In the first place, they cannot eat, or they will not eat, because they have the ulcer, and in the second place if they do eat, their gastro-intestinal tract is very efficaciously short-circuited in many cases and the food cannot go where it will be utilized.

I have found that many of them are dehydrated because they have a profuse

diarrhea I have encountered the most advanced cases of alkalosis that I have ever seen in this group of patients, and many of these patients have actually had clinical signs of scurvy. I believe that no group of patients deserves more careful preparation before operation than these cases. I cannot give you the exact mortality in our own patients prior to 1930, but it was high, probably about 40 per cent.

In 1930, we decided that we would spend a week or more in getting these patients ready, by transfusions and dietary regimen, high in vitamins, *etc*. Since that time we have operated upon 14 patients with gastrojejunocolic fistulae. In 1931, the first patient that we operated upon after we decided to spend this time in getting them ready died on the eighteenth day of a lung abscess. Our next patient died of peritonitis because of a leak from the anastomosis in the colon, but since that time we have had 12 patients upon whom we have carried out one-stage operations, all of them have recovered, I think largely due to the fact that we had prepared them very, very carefully, corrected their chemical abnormalities, brought their blood to normal, and taken plenty of time to do this before the operation was undertaken.

Every one of these patients presented lesions secondary to gastroenterostomy for duodenal ulcer. We try to restore the gastro-intestinal tract to normal, and we have done that in all of these patients that I mentioned. In three instances, the pylorus was closed by scar and we had to perform, in addition to the closure of the three involved organs, a pyloroplasty. All of them have done well except two, who have had a reactivation of their original duodenal ulcer. One of these was relieved by medical management, and I was obliged to perform a high resection of the stomach in the other.

I think if one will take plenty of time to prepare them and then utilize the operative principles of Allen and Pfeiffer, the results should be very much better.

DR CARL EGGERS (New York) About 12 years ago, a patient with an established diagnosis of gastrojejunocolic fistula came under my care. The symptoms were distressing. He complained chiefly of diarrhea, having to defecate as often as 12 times a day. As a result of this, emaciation was the outstanding manifestation. He weighed only 90 pounds. There were no ulcer symptoms. It appeared to us that closure of the communication with the colon was of the greatest importance. We realized that the patient would not be able to stand a prolonged operative procedure such as is required for separation of the stomach and intestine, with possible subsequent resection.

We therefore devised a method of less magnitude. Reasoning that the part of the colon which was attached to the stomach had become accustomed to receive acid gastric contents and would probably be able to protect itself against it in the future, we therefore divided the transverse colon proximal and distal to the fistula. After closing both ends, we left the midportion of the transverse colon as a permanent part of the stomach. The proximal and distal colon were united with an end-to-end suture, thus reestablishing normal continuity. The result was very satisfactory.

Some years later, however, the patient had recurrence of ulcer at the site of his original lesion in the duodenum with acute perforation. This was closed by suture.

Two years ago, he was admitted with acute intestinal obstruction due to carcinoma of the ascending colon. This was successfully resected.

DR FRANK H. LAHEY (Boston) It is obvious that this lesion, gastrojejunocolic fistula, has been a difficult one for us all to deal with. I think I should present our experience and the plan I recently devised to manage it, although it may not be the best one. None of us has had enough experience

with the newer developments in the management of these plans to really know yet which is the best one. I would like to discuss a plan which we have employed in two cases. Dr I. J. Walker, of Boston, who asked my advice concerning the management of such a lesion, has also successfully employed this procedure in a similar case of gastrojejunocolic fistula.

The thing that has bothered us in the management of the gastrojejunal ulcer is the peritoneal contamination which results from detaching the fistula into the colon. We have for some time sought for a plan to avoid opening the fistulous tract, but to permit resection of the stomach and jejunum. In these two cases the ileum as a preliminary measure has been cut across, the distal end closed and the proximal end implanted into the descending colon as a first-stage of the procedure. Then, at the end of two weeks, the ascending colon, the remaining terminal ileum, the fistula, the jejunum and the portion of the stomach to be resected are taken out in one block, and the end of the transverse colon distal to the fistula closed with the fecal stream already established.

This has been a very satisfactory method of handling this problem to avoid contamination, and although it sounds like an operation of tremendous magnitude, the colon is mobilized readily and it is not as difficult to perform as it seems.

DR DAMON B. PFEIFFER (closing). I appreciate these discussions and the additional value of the experience and suggestions made. I realize that the subject is not fully and finally settled by my observations, but it seems an inescapable conclusion that the three clinical observations here recorded throw a new light on the mechanism of the production of symptoms resulting from gastrojejunocolic fistula, and that a simple and safe method of rehabilitation is offered. The idea that the loss of health is due largely to escape of gastric contents directly into the colon seems untenable, because, in the first case, there was no such loss, as has been demonstrated roentgenologically, and to the failure of the food to pass into the colon after colostomy. In the second place, moreover, although some gastric contents did find their way directly through the fistula into the colon, it was found that after colostomy the same favorable effects occurred even though there was some continued passage of food into the colon. Although the bulk of the gastric contents passed into the small intestine, the same alleviation of gastric and colonic symptoms was noted. The third case bears out the same point. All this indicates that the disastrous effects of this type of fistula are due to passage of colonic contents into the upper gastrointestinal tract rather than the reverse. Exclusion is, therefore, the sound and simple method of bringing these cases back into a state in which the necessary complicated surgery may be accomplished with relative safety. It seems probable that resection, or resection by exclusion, may be the accepted method of dealing with these ulcer-ridden cases, and after complete rehabilitation this is not too dangerous a procedure.

I am lost in admiration of Doctor Collier's last series of 11 cases without a death. Doubtless with the newer methods of handling nutrition and fluid and chemical balance much can be accomplished without colostomy. It has not been our experience, however, even with the most strenuous efforts under hospitalization, that we have been able to improve the patient's condition to a satisfactory degree. Even if this can be accomplished, it would seem that the increased danger of performing radical surgery upon an area teeming with the bacterial flora of the colon must be greater than when this factor is eliminated. Certainly in cases which cannot be well controlled, the plan advocated will be found of value.

SCLEROSING OR RETRACTILE MESENTERITIS*†

ITS TREATMENT AND THAT OF ADHESIONS WITH THE ELECTROSURGICAL KNIFE

F L REICHERT, M D , F GERBODE, M D , AND F J HALFORD, M D

SAN FRANCISCO, CALIF

FROM THE LABORATORY OF EXPERIMENTAL SURGERY, STANFORD UNIVERSITY SCHOOL OF MEDICINE, SAN FRANCISCO, CALIF

THICKENING and shortening of the mesentery, with great distention of the lymphatics in the involved mesentery and bowel, were observed when we ligated in continuity all the vessels, artery, vein and lymphatics, to a small segment of bowel. The same result occurred when the lymphatics to the segment were ligated. The ligations were made in the region of the second and third branching. The bowel itself showed very little alteration except possibly a little thickening.

This retraction and thickening of the mesentery reminded us of certain clinical cases, infrequently seen, in which certain areas of the mesentery were found thickened and retracted.

In the paper by Reichert and Mathes¹ on experimental lymphedema of the intestinal tract and its relation to regional cicatrizing enteritis, Case 3 (M P) was that of a man who had suffered a severe blow on the abdomen from the steering wheel of an automobile. He was operated upon two months later for intestinal obstruction. An area of ileum was found bound down and kinked. The mesentery was very short, boggy and thick. At one point in its root, a small mass of dark colored material, either fecal matter or old, unabsorbed blood pigment, was found. Resection of the involved bowel and mesentery cured the condition. The pathologic study of the resected ileum showed chronic ileitis with the submucosa greatly thickened and edematous. The lacteals between the muscular layers were greatly engorged and many were thrombosed.

Another patient (M H), a boy, age 14, two years before entry had had acute appendicitis with possible rupture. Appendicectomy with drainage was performed at another hospital. He remained well until two months before admission, when his first and only attack of cramps, in the right lower quadrant, and soreness developed. Hot stupes and manipulation of the abdominal wall with the patient in the knee-chest position relieved the pain. A diagnosis of intra-abdominal adhesions was made. At operation omental adhesions to the cecum and terminal ileum were freed with the electrosurgical knife. A fibrous band, 3 Mm thick and 4 cm long, extending from ileac wall to terminal ileac wall, so arched the bowel that a loop of intestine could easily slip between and cause obstruction. The terminal ileum was narrowed and angulated by fibrous contracture of the mesentery. The regions with narrowing, angulation and

* Aided by a grant from the Fluid Research Fund of the Rockefeller Foundation

† Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

contracture were released by lightly coagulating the scar tissue and letting it pull apart. The bowel wall was somewhat thickened, probably from the scarring and retraction of the mesentery with lymphatic block, rather than being a true regional ileitis.

We reviewed the work of Welch and Mall² on hemorrhagic infarction but could find only an occasional mention of the lymphatics and none of mesenteric retraction among their many beautiful experiments.

Our search in the modern text-books of surgery revealed no mention of retractile mesenteritis, *per se*, although great thickening of the mesentery was discussed under the recently described condition of regional enteritis.

In Volume 4 of Keen's System of Surgery, 1908, Van Hook and Kanavel describe contraction of the mesentery and quote the observations of O. Brehm,³ who felt that mesenteric shrinking was not only to be regarded as an etiologic factor in volvulus of the sigmoid but also as a disease, *sui generis*, which demanded treatment. He felt that simple detorsion of angulated loops did not suffice in mesenteric contraction and that radical resection was necessary.

A number of papers on retractile mesenteritis have appeared in foreign literature during the past ten years. In Bonorino's article⁴ on sclerotic and retractile mesenteritis he gave credit to Virchow⁵ for describing sclerotic mesenteritis of the sigmoid flexure, in 1853. Virchow believed that a circumscribed peritonitis with cellulitis and sclerosing degeneration in the mesentery caused its retraction, this retraction being necessary in the production of volvulus of the pelvic colon.

Subsequent to the appearance of Virchow's paper, authors have reported one or more cases of retractile mesenteritis. Tuberculosis by some, trauma by others, was considered to be the causal agent. In reviewing the case reports in the literature and those collected by Bonorino up to the year 1929, we did not feel that the descriptions were entirely similar to the condition now considered as regional enteritis.

Apparently the first experimental work on retractile mesenteritis was reported in 1927 by Jura⁶ who, by injecting bacteria from the intestinal flora into the mesentery of the ileum, produced a lymphangitis and subsequent retractile mesenteritis.

Stropeni,⁷ in 1933, from experiments on dogs, stated that when the mesenteric veins were ligated or injected, mesenteritis developed. He did not find any disturbance when the artery was ligated. No animals showed any infiltration of lymphatics and he concluded that trauma produced mesenteritis by interference with veins.

Milone and Picco,^{8, 9} in a preliminary note in 1933, and a complete report in 1935, discussed in detail the many and varied theories in the literature as to the etiology of retractile mesenteritis. They believed that disturbance of lymphatics caused retraction of the mesentery because absorption from the intestines was greater in lymphatics than in veins, and lymphatics were more

readily disturbed. In their experiments on rabbits they tied off the lymphatic trunks at the root of the mesentery without injuring the arteries and veins. Histologic study, one to 60 days after operation, showed that retractile mesenteritis did not develop until about the tenth day, and that the changes produced by blocking lymphatics passed through the following three stages. Diffuse edema of the mesentery with mobilization of migratory elements, especially the histocytes, first occurred. This was followed by hyperplasia of the connective tissue from new fibroblastic proliferation—at first fibrillary, then circumscribed in bundles and bands perpendicular to the direction of the lymphatics. The third stage consisted of sclerosing of newly formed connective tissue bundles and cords with gradual replacement by collagen fibers and eventual retraction of the mesentery. They concluded that the cause of mesenteritis was of intestinal origin, that it was linked with the intestinal substances of attenuated organisms of undetermined nature which penetrated the intestine through the veins or lymphatics, or were held in them in a relatively higher concentration by obstacles causing obstruction, such as hematoma after trauma, inflammation or neoplasm.

Thus in the experimental work of Jura, Stropeni, and Milone and Picco, retractile mesenteritis was produced by mesenteric inflammation from bacteria, or from ligating mesenteric veins or lymphatics. It was not produced by ligation of the mesenteric artery.

This previous experimental work on mesenteritis seemed inconclusive since the components of the circulatory system in the mesentery had not been studied in the same animal individually and collectively. From our earlier work on lymphedema¹ we knew of the fibrosis and scarring that developed when the lymphatic system was blocked in the bowel and in the mesentery, but we did not emphasize this finding since small amounts of the sclerosing solution leaking into the mesentery from the punctured lymphatics might have been a factor in causing the retraction.

Experimental Investigation—The experiments we are now reporting concern circulatory imbalance in the canine mesentery. They can be divided into seven parts, namely, the effect produced by (1) ligating all structures, artery, vein, nerve and lymphatics, in a segment of the mesentery proximal or distal to the second branching from the root of the mesentery, (2) ligation at this level of the artery and vein, (3) ligation at this level of the lymphatics, (4) ligation at this level of the artery, (5) ligation at this level of the vein, (6) the formation at this level of hematoma in the mesentery, and (7) trauma to the mesentery.

Early in the experimentation it was realized that a number of factors must be controlled if the results were to be interpreted as being due only to the experimental procedure. Study of the protocols of the first two animals showed the necessity of assistance during the operation and of the utmost care in handling the bowel. Perhaps the greatest factor to interfere with the estimation of results was adhesions which developed when small amounts of

blood soiled the abdominal contents, or when all the talc on the gloves had not been washed off. Adhesions also developed after frequent sponging with moist gauze or when drying of the exposed bowel and mesentery occurred. As the investigation progressed it became evident that the proper treatment of adhesions was another interesting problem which will be discussed later. Photographs were taken at the operating table when reopening the animals for observations, since the alterations could not be seen well in the sacrificed animal. But the photography had to be abandoned as the drying of the exposed bowel by photo-flood lamps produced adhesions.

A summary of the experiments is given in Table I. In a single animal three to eight different ligations have been performed at stated points in the mesentery of the small bowel. Between ligations normal or control segments of mesentery intervened. When no alteration in the mesentery was found at exploration, one to eight weeks later it was indicated as 0 in the table. Shortening and thickening of the mesentery was indicated as + in the table.

It will not be necessary to give the protocols of each animal, but that of Dog 11 will suffice to outline the procedure and present the findings.

TABLE I
EXPERIMENTS ON PRODUCTION OF RETRACTILE MESENTERITIS AND ITS TREATMENT

Dog	Lym- phatics Ligated	All Vessels Ligated	Artery Ligated	Vein Ligated	Artery and Vein Ligated	Hema- toma	Hema- toma + Irrita- tion	Irrita- tion	All Vessels Ligated at Root	Remarks
1	+	0		+	0					
2	0?	0?	0?	0?						
3	+	+		0						
4		+	0	0	0				+	
5	+	+	0							
6		+	0		0					
7	0	+	0							
8	0	+	0	0	0	0			0	
9	+	+	0	0	0	0			0	Electrosurgical R No reformation
10	+		+	0	0					
11	+	+	0	0	0	0			+	
12		Died 10 hrs p o								
13	?	?	?	?						Loops of bowel matted together
14								+		Electrosurgical R No reformation
15								+		Electrosurgical R No reformation
16								+		
17	+							0		Electrosurgical R No reformation
18		+					0	0		
19	+	+					+			Scissors R More exten- sive reformation
20								+		Scissors R More exten- sive reformation
21								+		Scissors R Reformation
22								+		Scissors R Reformation

+ Shortening and thickening of segment of mesentery

0 No change

? Adhesions obscured observations

RETRACTILE MESENTERITIS

Protocol of Dog 11—This adult female had the following experiments started, November 7, 1938

(1) On November 7, 1938, all vessels, artery, vein and lymphatics, proximal to the third branching of a segment of the mesentery were ligated together, in continuity, with black silk. On November 18, 1938, at exploration, retraction and thickening of the mesentery was found (Fig 1 [II]). There were no adhesions.

(2) After leaving an adjacent normal segment of mesentery as a control a hematoma, 2 cm in diameter, was produced between the leaves of the mesentery at the third branching by needling the vein. On November 18, 1938, the hematoma had been absorbed and no change was found in the mesentery (Fig 1 [III]).



FIG 1—Dog 11. Photographs of ligated regions of mesentery 11 days after operation. (I) All vessels ligated in continuity producing retraction of segment of mesentery. (II) Mesenteric hematoma absorbed and no alterations in mesentery noted. (III) Artery and vein ligated but no alteration in mesentery seen.

(3) An adjacent portion of the mesentery was left for control and then the artery and vein at the third branching were ligated together in continuity. On November 18, 1938, no change was observed in the mesentery or bowel (Fig 1 [III]).

(4) After another control segment of mesentery was left, the artery, vein and lymphatics were ligated together in continuity at the third branching. On November 18, 1938, shortening and thickening of the mesentery and slight thickening of the bowel were found (Fig 2 [IV]).

(5) After leaving an intervening control segment of mesentery the lymphatics only were ligated in continuity at the third branching. A note was made that the accompanying artery and vein were not constricted. On November 18, 1938, slight but definite retraction of the mesentery was observed (Fig 2 [V]).

(6) The vein was ligated at the third branching after leaving a segment of mesentery as a control. On November 18, 1938, no change was noted in the mesentery (Fig 2 [VI]).

(7) The lymphatics only were ligated at the first branching after leaving a segment of mesentery as a control. The accompanying artery and vein were patent. On November 18, 1938, thickening and retraction of the mesentery and thickening of the bowel wall were found (Fig 2 [VII]).

(8) A segment of mesentery was left as a control and then the artery alone was ligated at the second branching near the terminal ileum. A small hemorrhage in the mesentery occurred at the time

of ligation On November 18, 1938, the hemorrhage had been absorbed and no alteration was noted in the mesentery A small omental adhesion was found on the bowel near this region

The animal was sacrificed, January 20, 1939, at which time many omental adhesions to the small bowel were found They probably were caused by exposure and drying of the bowel and mesentery during photography

Summary of Experimental Results—The experimental findings in 22 animals may be followed in Table I

The lymphatics in a segment of the mesentery were ligated in 11 experiments In seven, there was definite shortening and thickening of the mesentery and one showed dilated lymphatics but no retraction



FIG 2—Dog 11 Ligated regions of mesentery 11 days after operation (IV) All vessels ligated producing retraction and thickening of the mesentery (V) Some retraction occurred after ligation of lymphatics alone (VI) No change seen after ligation of the vein (VII) Retraction of mesentery and slight thickening of bowel after ligation of lymphatics at second branching

All vessels—artery, vein and lymphatics—in a segment of the mesentery were ligated in 12 experiments In ten, definite retraction of the mesentery occurred

When only the artery was ligated, no retraction occurred in eight experiments In one, a questionable shortening of the mesentery was seen beneath an omental adhesion

When only the vein was ligated, no change in the mesentery was noted in seven experiments In one, the mesentery was thickened and the omentum was adherent to the site of the ligation

Hematomata were produced in the mesentery in three experiments but no retraction occurred. In two other experiments, in which a hematoma was produced and the mesentery overlying the hematoma was rubbed with gauze, one showed retraction of the mesentery. All hematomata were quickly absorbed.

When the mesentery was irritated with talc from gloves or by rubbing it with gauze, retraction occurred six times in eight such experiments. Ligation of all vessels at the root of a segment of mesentery produced retraction twice in four experiments.

We, therefore, found that retractile mesenteritis could be produced consistently when all vessels in a segment of the mesentery near the third branching were ligated. Usually, it could be obtained when the lymphatics alone were ligated or when the mesentery had been irritated or traumatized. It did not occur when the artery or the vein, or when both artery and vein, were ligated. Hematomata in the mesentery were absorbed and produced no retraction.

We agree with Milone and Picco^{8,9} that the lymphatic stasis plays an important part in the production of retraction of the mesentery.

Careful histologic study of the mesentery and bowel in Dogs 8, 9, 17 and 19 confirmed, in general, the findings of Milone and Picco. In the later stages, that is, two or more months after ligation, we found an increase of fibroblasts and elastic tissue fibers just beneath the serosa, where they formed an irregular sheet from which long fibrous strands extended interiorly. Around some of the mesenteric vessels the van Giesson stain showed a slight increase of fibroblasts. This fibrosis, limited to the outer or superficial part of the mesentery, produced the retraction. No definite alteration was seen in the deeper areolar and fatty portion of the mesentery. In some experiments, where all vessels in a segment of mesentery were ligated, the bowel showed slight thickening, with dilation of the lacteals and edema in the musculature.

Treatment of Retractable Mesenteritis—The older writers advised radical resection for retractile mesenteritis, and this seemed the only feasible procedure when the condition was extensive with angulation of the bowel, such as was found in our first case.

In our experiments, and in our second case, where the retraction was moderate and the bowel in good condition, satisfactory treatment consisted of dividing adhesions and freeing the scarred contracted mesentery with the electrosurgical knife.

Clinically, we have preferred the division of adhesions after the method of Trowbridge¹⁰ who, in 1929, advised treating them with the electrosurgical knife.

In seeking proper treatment for retractile mesenteritis in animals, this method of Trowbridge's seemed to be advantageous as compared with the customary freeing of scars and adhesions with the scalpel or scissors.

Although this comparison in the treatment of retractile mesenteritis and

of adhesions was made in only eight experiments, definite conclusions could not be drawn at this time since we had not compared the two methods in the same animal

Treatment by division with the scalpel or scissors of omental and mesenteric adhesions and of retractile mesenteritis was employed in four animals. No attempt was made to peritonize the raw surfaces. Subsequent explorations showed, in all four animals, reformation of adhesions and more retraction of the mesentery. In two, the adhesions were more extensive after this form of treatment.

Employment of the electrosurgical knife, set for slow coagulation, was used to separate and free omental and mesenteric adhesions and retractile mesenteritis in four other animals. Separation was made with ease by keeping the adherent areas under slight tension. Subsequent exploration showed that the adhesions had not reformed in the cauterized areas, and the sclerosed mesentery showed no or only slight retraction.

Protocol of Dog 9—An adult female, the following are the findings after the use of the electrosurgical knife to separate adherent areas:

(1) On October 26, 1938, all vessels were ligated in continuity in a segment of the mesentery at the third branch. On November 3, 1938, the mesentery was found retracted. There were no adhesions. On December 5, 1938, the fine mesenteric scars were separated by electrocoagulation. On December 12, 1938, no adhesions and no retraction was found. On January 20, 1939, no adhesions and no retraction was seen.

(2) On October 26, 1938, the lymphatics only were ligated in a segment of mesentery. On November 3, 1938, the mesentery was found shortened and thickened with dilated lymphatics on the surface of the involved bowel. No adhesions were present. On December 5, 1938, both sides of the contracted mesentery were touched lightly with the electrosurgical knife. On December 12, 1938, and January 20, 1939, no retraction had recurred and there were no adhesions.

(3) On October 26, 1938, the artery alone was ligated at the third branching. On November 3, 1938, no changes were found. On December 5, 1938, small collateral arterial vessels had developed around the point of ligation. On December 12, 1938, and January 20, 1939, no further changes had occurred.

(4) On October 26, 1938, the vein was ligated at the third branch. On November 3, December 5, and 12, 1938, and January 20, 1939, no changes were seen.

(5) On October 26, 1938, the artery and vein were ligated together. On November 3, December 5, and 12, 1938, and January 20, 1939, no alterations were noted.

(6) On October 26, 1938, a hematoma, about 2 cm. in diameter, was produced between the third and fourth branchings. On November 3, 1938, slight infiltration and discoloration was noted. On December 5, 1938, this region appeared to be normal and continued so when observed, December 12, 1938, and January 20, 1939.

(7) On October 26, 1938, three hematomata were produced between the fourth and fifth branchings near the mesenteric attachment to the bowel. On November 3, December 5 and 12, 1938, and January 20, 1939, the area appeared to be normal.

(8) On October 26, 1938, all vessels at the second branching were ligated. On November 3, 1938, there was no retraction, but lace-like opaque areas were seen on the mesentery. On December 5, 1938, scars were divided with the electrosurgical knife. On December 12, 1938, and January 20, 1939, a slight decrease in amount of scarring was noted.

Comments on Protocol of Dog 9—At the first operation extreme care was taken in handling the bowel and in keeping it moistened with warm normal saline. Gauze was applied only once to the mesentery to control oozing at the site of a hematoma. On December 5, 1938, at the third operation in the region where the fourth, fifth and sixth ligations were made, a large omental adhesion was attached to the bowel wall for a distance of three inches. This adhesion was freed from the bowel by electrocoagulation (Fig. 3). In

RETRACTILE MESENTERITIS



FIG 3—Dog 9 Shows division of adhesions with electro-surgical knife



FIG 4—Dog 9 January 20 1939 Upper indicator lies over normal bowel to which omentum had been adherent. Bowel freed from omentum with the electro-surgical knife one month previously. A new omental adhesion had developed to normal adjacent bowel. The lower indicator points to a free strand of omentum which had been freed from the mesentery one month before by means of the electro-surgical knife

order to identify the areas divided, a black silk tie with ends 5 mm long was placed on the bowel where the omentum was freed. Another similar tie was fastened to the omental stump. The same treatment and similar identification marks were applied to another small omental adhesion attached to a small area of mesentery. On December 12, 1938, at the fourth operation, the small bowel showed slight scarification of the serosa over the area freed from the omental adhesion. A pencil-like strand of omentum was attached to the black tie on the bowel. Another end of omentum had attached itself to the black tie on the mesentery where the other adhesions had been freed. This formation of adhesions to the knot area has just been described in the experiments of Donaldson and Cameron¹¹. On January 20, 1939, the abdomen was opened and observation and photographs made. Wherever electrocoagulation had been used no adhesions were found. Where the retracted mesentery had likewise been freed, scarring was present but no retraction persisted. The only indications of electrocoagulation were several small yellowish scars in the serosa. The area of bowel to which the omentum had been adherent showed no adhesion or scarification, and is indicated in Figure 4 by the match-stick on the bowel. One new adhesion had formed near this area on normal bowel, probably from trauma and exposure. The other match-stick points to a free omental tag previously separated from the mesentery by electrocoagulation.

Although these experiments on the treatment of mild retractile mesenteritis and of adhesions are not conclusive, they at least suggest that electrosurgical division of adhesions is far superior to the customary division with scalpel or scissors. Apparently division by coagulation leaves dead tissue on the exposed surface with healing occurring beneath before separation of the scar. This would prevent new points of adhesion.

CONCLUSIONS

Retractile mesenteritis is no longer mentioned in the modern text-books of surgery.

Retraction of the mesentery is discussed in texts, as occurring in the recently described condition of regional enteritis.

One of our cases with retractile mesenteritis has been reported as a case of regional enteritis. The other case also might be considered as a mild instance of regional enteritis.

European investigators have reported experiments in which retractile mesenteritis was produced by mesenteric inflammation from bacteria, or by ligating mesenteric veins or lymphatics.

We found that retractile mesenteritis could be produced consistently when all vessels in a segment of the mesentery were ligated. Usually it could be developed when the lymphatics alone were ligated or when the mesenteric leaves had been irritated or traumatized.

Our experiments indicated that lymphatic stasis played an important part in the production of retraction of the mesentery, since it did not occur when the artery and vein, or each alone, were ligated.

Since mild degrees of retractile mesenteritis were produced experimentally, radical resection was not considered as the proper treatment

In the treatment of experimental retractile mesenteritis and intra-abdominal adhesions, the electrosurgical knife was found to be superior to the customary division with scissors or scalpel

REFERENCES

- ¹ Reichert, F L, and Mathes, M E Experimental Lymphedema of the Intestinal Tract and Its Relation to Regional Cicatrizing Enteritis ANNALS OF SURGERY, 104, 601, October, 1936
- ² Welch, W H, and Mall, F P Experimental Study of Haemorrhagic Infarction of the Small Intestine in the Dog Papers and Addresses by William Henry Welch The Johns Hopkins Press, Baltimore, 1, 77, 1920
- ³ Brehm, O Uber die Mesenterialschrumpfung und ihre Beziehungen zum Volvulus der Flexura sigmoidea Arch f klin Chir, 70, 267, 1903
- ⁴ Bonorino, Udaondo C Las mesenteritis esclerosantes y retractiles Prensa Med Argent, 16, 233, July 20, 1929
- ⁵ Virchow, R Historisches, Kritisches und Positives zur Lehre der Unterleibsaffektionen Virchow's Arch f path anat u physiol, 5, 281, 1853
- ⁶ Jura, V Sulla mesenterite retractile e slerosante Policlin, Roma, 31, 575, 1924
- ⁷ Stropeni, L Ricerche sperimentali sulla patogenesi della mesenterite retractile Boll e mem Soc piemontese di chir, 3, 668, 1933
- ⁸ Milone, S, and Picco, A Sulla patogenesi della mesenterite retractile (Nota preventiva) Boll e mem Soc piemontese di chir, 3, 1069, 1933
- ⁹ Milone, S, and Picco, A Sulla patogenesi della mesenterite fibrosa retractile Arch ital di chir, 39, 117, 1935
- ¹⁰ Trowbridge, E H Treatment of Abdominal Adhesions by Use of the Electrosurgical Knife New Eng Jour Med, 201, 1183, December 12, 1929
- ¹¹ Donaldson, J K, and Cameron, R R A Study of the Use of Silk, Catgut, and the Noble Plication with Reference to Abdominal Adhesions Surgery, 5, 511, April, 1939

DISCUSSION—DR JOHN HOMANS (Boston) Doctor Reichert's skill with the fine needle has led him into a field into which very few of us are able to follow He was able experimentally, for instance, to reproduce, in a very practical way, what seems to have been a regional enteritis, and not satisfied with that, he has refined his experiment and produced chronic thickening in the mesentery by what seem to be impossibly simple means

In that respect, it is rather interesting to speculate upon why lymphatics behave in this way, and that is my excuse for discussing this paper, for I know nothing whatever about the cicatrizing changes in the mesentery I take it that most of us would notice them if our eyes were open to them, but apparently we have not taken much note of them

If lymphatics are divided on a large scale, as in experiments which Doctor Reichert performed years ago, and the whole leg is encircled by an incision, they find no difficulty in crossing the scar, but apparently they are very subject to disorganization for other reasons If, for instance, one plugs up the lymphatics over a considerable area, they appear to go to pieces and the tissues which they drain tend to become first edematous and then indurated by the formation of new tissue

Doctor Homans then showed a drawing made from a roentgenogram, taken following the injection of lipiodol, demonstrating the veins of the dog's leg, with the lymphatics outlined in black One could see, at a point behind the knee, a lymph node with a large number of entering vessels, and at a

point nearer the body, a place where one ought to be able to interrupt most of the large lymphatics

A second roentgenogram was shown of an animal whose principal lymph vessels had been tied off. Perhaps ten days or a week afterward, the animal was given thoriatrast in its paw, which demonstrated the lymphatics, which appeared to be quite orderly vessels of rather large size.

Apparently, with time, these obstructed vessels dilate, losing the use of their effective valves, which was demonstrated by a roentgenogram taken some four or five weeks afterward, in which one could see traces of the thoriatrast and perhaps the remains of the larger vessels, as if they were dilated and had succeeded in absorbing only a very little thoriatrast.

Doctor Homans took this to indicate that once the lymphatics have been interrupted and have been unable to reform, they tend to become disorganized, and perhaps that is the reason why, for anatomic reasons, of which we know very little, in certain parts of the body, possibly because of the presence of terminal vessels, quite remarkable effects can be produced by division of these vessels.

Of course the by-product of this investigation was perhaps as interesting a part of it as any, namely, that the division of adhesions by the coagulating current was a very efficient way of dealing with intraperitoneal bands.

DR ARNOLD SCHWYZER (St Paul, Minn.) I was impressed when I heard that simple ligation of the lymphatics in the mesentery causes retractile mesenteritis. We all have seen in cases of appendicitis in the lowest ileum loop now and then a marked retraction of the mesentery, but where is the origin of a regional ileitis or a retractile mesenteritis farther up? That could be a problem.

I saw two cases which might give a clue, and that is why I rose. The two cases, one a very recent one, were of acute appendicitis, and in both instances was found a large abscessed node at the root of the mesentery. Now, you would expect that these nodes would be located right at the ileocolic junction, but nothing of the kind. There was no direct connection between the appendix and the abscessed nodes, which in one case was in the midline above the promontory. In the second case, it was even a little to the left of the midline. I suppose that the whole area of lymphatics was affected and over the lumbar vertebrae some mechanical damage was added, which caused a breaking down of a node with abscess formation.

In this way, one can think that even farther up on the ileum an appendiceal infection may be the primary cause of a regional ileitis and retractile mesenteritis.

DR MARTIN B. TINKER (Ithaca, N. Y.) I would like to discuss electrosurgery in abdominal cases. There must be several here who attended the symposium at the College of Surgeons in Philadelphia some five or six years ago, at which the question of electrosurgery was discussed and its advantages were brought forward. It seems that the men who have profited most by using electrosurgery have been interested in neurologic surgery, and who, with Cushing's lead, have used it very extensively.

I have been impressed, however, with its value in abdominal conditions, such as Doctor Reichert mentioned. Three patients who came in with recurrent intestinal obstruction had been operated upon two and three times before, without permanent results the obstruction recurring. It seemed that the more favorable results following electrosurgery in freeing adhesions in these cases was the factor that gave permanent results. In several cases they have remained well two and three years following operation, or longer, where

recurrence had followed promptly previously. Doctor Reichert's experimental studies confirm and explain clinical experience.

DR JOHN A. WOLFER (Chicago) I believe we all recognize that the lymphatic system, especially as it exists in the mesentery of the bowel, is a very complex one. I believe it has been proven by a number of men that if dyes or opaque materials are injected into a segment of bowel or its mesentery, and the lymphatics in the immediate zone are obstructed, that the opaque materials take a rather circuitous route and eventually arrive in the main lymphatic channels or nodes proximal to the site of obstruction. I am wondering if the fact that there is a very rich collateral lymphatic circulation in the mesentery was taken into consideration in arriving at conclusions.

DR F. L. REICHERT (San Francisco) I wish to thank the members for their discussion and to answer Doctor Wolfer's question. The amount of bowel involved in a ligation usually was between two and three inches, and from our previous work we felt that this degree of involvement took in all of the lymphatics of that part. Of course there is anastomosis on either side. That also developed when we ligated all of the structures in that region.

LIVER TRAUMA AND THE HEPATORENAL SYNDROME*

THOMAS G ORR, M D , AND FERDINAND C HELWIG, M D

KANSAS CITY, KANS

FROM THE UNIVERSITY OF KANSAS HOSPITALS, KANSAS CITY, KANS

THE IMPORTANCE of the toxic effect of liver trauma upon the kidneys was first emphasized by F C Helwig and his associates^{1, 2, 3} At the time of their studies in 1932, a case was reported in which the important observations of interest were a traumatic necrosis of the liver with extensive retention of creatinine, and a high grade nephrosis The patient was a boy, age 15, who had received a severe automobile injury He died 11 days following the accident His principal clinical symptoms were a temperature of 102.8° F, vomiting, secondary anemia, leukocytosis, jaundice, almost complete suppression of urine, generalized edema, moderate abdominal distention, and red blood cells and albumin in the urine The nonprotein nitrogen was 240 mg and the creatinine 25 mg per 100 cc of blood before death Operation on the sixth day revealed a large quantity of bloody, bile-stained fluid in the abdomen An autopsy showed a large area of pulpified liver tissue in the right lobe, large swollen kidneys, blood- and bile-stained ascitic fluid, bloody fluid in the pleural cavities, parenchymatous and subpleural hemorrhages in the lung, and subserous and submucous hemorrhages in the large intestine Microscopically, the damaged liver showed extensive necrosis The pathologic changes observed in the kidneys were leukocytic infiltration in the medullary portion, interstitial hemorrhages, dilated small vessels, red cells in the tubules of the medulla, cloudy swelling, albuminous precipitate and pale casts in the collecting tubules, parenchymatous degeneration in the convoluted tubules and loops of Henle swelling of the glomerular epithelium with red cells between the tuft and capsule, and polymorphonuclear leukocytes in the capillary channels

At the time of the above report, only one case of liver trauma was found recorded in the literature, which had been carefully studied from the standpoint of its relation to kidney damage Fuitwaengler⁴ reported this case in 1927, from Professor Clairmont's Clinic in Zurich He described a diffuse cortical necrosis of both kidneys following a severe injury to the liver, which resulted in death in three days He recognized the relationship between liver damage and renal necrosis and explained the latter on the basis of an ischemia produced by a chemical toxin liberated in the blood stream as a result of decomposition of hepatic tissue He believed that vascular spasm followed by ischemia produced the renal necrosis Henschen⁵ mentions that Volkman-Munster has seen a case of gunshot wound of the liver and that he has observed a case of liver rupture, both of which died of lipoid degeneration of the kidneys

* Read before the American Surgical Association, Hot Springs, Va, May 11, 12, 13, 1939

In 1930, McKnight⁶ reported a case of severe liver trauma which had a blood urea as high as 268 mg per 100 cc of blood. The urine on admission was entirely normal but at various times later showed sugar, albumin, and hyaline and granular casts. He considered the high blood urea as evidence of gastrointestinal stasis and mentioned that it might have been associated with renal impairment. In 1930, Stanton⁷ also recorded the case of a young man who died 47 hours after a traumatic rupture of the liver with a temperature which reached 105.6° F in 22 hours after the accident. He remarks that this case presented a clinical picture similar to that seen in the rapid deaths following gallbladder operations and was inclined to believe that similar factors were operative in his case. No blood studies were made and no pathologic changes in the kidneys were mentioned. In 1934, Rosenbaum⁸ observed a patient with lethal anuria following liver rupture. His patient was a male, age 65, who died 30 hours following an accident. Extensive epithelial degeneration was found in the collecting tubules of the kidneys. Death was attributed to nephrosis with anuria. Helwig and Schutz⁹ added another case report in 1935. The patient was a male, age 61, who had been injured in an automobile accident. His principal signs and symptoms were pain in the right chest, a temperature which ranged from 99° to 102° F, tenderness over the right ribs and right abdomen, abdominal distention, slight edema, diminished urinary output, and albumin, hyaline casts, and red blood cells in the urine. On admission to the hospital soon after the injury, the urine, blood, and blood chemistry were normal. The third day after the accident the blood nonprotein nitrogen was 75 mg and the creatinine 3 mg per 100 cc. At autopsy extensive laceration of the liver with some pulpefaction was found. The liver cells showed varying stages of necrosis and disintegration. Cloudy swelling, vacuolar degeneration, and loss of nuclei of the tubular epithelium were the outstanding histologic changes in the kidneys. In a general discussion of "liver death" in 1935, Boyce and McFetridge¹⁰ recorded three cases of gunshot wound of the liver and one case of liver injury due to automobile accident in which the temperature reached 105.4° to 108.2° F. These patients all died, but no pathologic studies were made. Two other cases of severe liver injury following automobile accidents revealed at autopsy typical degenerative changes in both liver and kidneys. In one of these cases the jaundice was quite marked with an icteric index of 210. Becker¹¹ reports a case from Henschen's Clinic in Basel. His patient was a male, age 27, who had been injured in an automobile accident. The patient died six hours following operation, in less than 24 hours following the injury. A large laceration was found in the right lobe of the liver. Microscopic examination of the kidneys showed parenchymatous degeneration of the cortex and necrosis of the epithelium of the convoluted tubules. He attributed these changes to a pathologic relationship between the damaged liver and the kidneys. Blood studies were not recorded.

Five cases of liver injury associated with kidney damage are reported herewith. Four cases were studied in the University of Kansas Hospitals, Kansas City, Kansas, and one in St. Luke's Hospital, Kansas City, Missouri.

CASE REPORTS

Case 1—E T, white, male, age 17, was injured in an automobile accident, December 18, 1932. He was admitted to the hospital at once, in a mild state of shock with tenderness and rigidity of the right upper abdominal muscles. Three hours after the accident he was operated upon and a deep laceration was found in the inferior surface of the right lobe of the liver. There was a large quantity of blood in the abdomen. The wound in the liver was packed with gauze and the abdomen drained. With multiple transfusions his condition improved. He was delirious for three days. A *Streptococcus hemolyticus* infection developed in his wound which delayed recovery. At the end of four weeks an empyema was drained which showed a culture of *Staphylococcus aureus* and *Staphylococcus hemolyticus*. During the height of his infection his fever reached 104° F. He recovered and was discharged from the hospital at the end of three months.

The urine contained albumin and pus cells. Blood chemical studies on the day following the injury showed a nonprotein nitrogen of 82 mg and creatinine of 4 mg per 100 cc. These changes returned to normal on the fourth postoperative day (Table I). The second day following the accident the icteric index was 10.

Case 2—T J, male, age seven, was struck by an automobile, May 16, 1933. He was brought immediately to the hospital in a profound state of shock. There were abrasions on the right abdominal wall, forehead and leg. Some blood cells were found in the urine. His general condition improved with transfusions and infusions. Restlessness and delirium were marked symptoms throughout his illness. An abdominal exploration was made 24 hours after the accident. The abdomen was filled with blood. A deep laceration was found extending far back into the inferior portion of the right lobe of the liver. There was some retroperitoneal hemorrhage about the right kidney. Bleeding from the liver was controlled with a gauze pack. The highest temperature recorded during the first three days was 105.4° F. A slight cyanosis developed and oxygen therapy was given. Infection developed in the wound which showed a *Staphylococcus aureus* and a nonhemolytic *Streptococcus*. During the course of the illness blood cells in the urine decreased and coarsely granular casts and occasionally a few pus cells appeared. Granular casts were found in the urine throughout the illness. The blood count showed a leukocytosis and secondary anemia. The day after injury the nonprotein nitrogen reached 131 mg and the creatinine 41 mg per 100 cc of blood. Changes in blood chemistry returned to normal on the sixth day of the illness (Table I). Death occurred on the eleventh day following the injury. Autopsy showed an irregular laceration 12 cm long in the superior portion of the right lobe of the liver extending through to the inferior surface. There were also infarction and early pulpification of the liver, thrombosis of the renal veins with infarction of the right kidney, compensatory hypertrophy of the right kidney, perirenal hemorrhage, hemopericardium, acute serofibrinous pleurisy, atelectasis of the lungs and acute generalized peritonitis.

Pathologic histology of the injured area of the liver revealed marked necrosis, vacuolization of liver cells, edema, infiltration with polymorphonuclear and mononuclear leukocytes, proliferating bile ducts and organizing exudate on the surface. The changes in the kidneys were cloudy swelling, distention of convoluted tubules, congestion of glomerular tufts, hemorrhages in the medulla, hyaline casts in the tubules, edema, atrophy of some of the convoluted tubules, some infiltration with mononuclear leukocytes, occasional polymorphonuclear leukocytes in the collecting tubules, coagulation necrosis in the infarcted area of the kidney, and thrombi in the renal veins.

Case 3—R V H, white, male, age 23, was injured, June 27, 1933, by being thrown from a truck. He was admitted to the hospital within two hours, in a state of shock. Examination revealed a fractured rib, subcutaneous emphysema, abrasions of the right leg, and tenderness and rigidity over the right upper abdomen. Blood was found in the urine. Roentgenograms showed partial collapse of the right lung. Two transfusions were given and at the end of nine hours after the injury the abdomen was explored. The

THE HEPATORENAL SYNDROME

TABLE I

BLOOD CHEMICAL STUDIES IN FIVE CASES OF HEPATIC TRAUMA

Case No	Day after Injury	Nonprotein Nitrogen Mg per 100 Cc of Blood	Creatinine Mg per 100 Cc of Blood	Sugar Mg per 100 Cc of Blood	Carbon Dioxide Combining Power Volume Per Cent	Whole Blood Chlorides	Remarks
1	1	82.5	4.0	100	41	490	Operation 3 hrs after injury First blood study 36 hrs after injury Recovery
	2	79.8	2.0	77	43	490	
	3	68.3	1.9	99	33	550	
	4	34.0	1.5	153	46	580	
	5		1.5	83		500	
2	0 A M	68	2.1	101		550	Operation 24 hrs after injury First blood study 15 hrs after injury Death
	0 P M	58	2.3	132		520	
	1	131	4.1				
	2 A M	98	3.3	118		560	
	2 P M	62	2.7				
	3	71	2.8	145	33	590	
	4	53	1.9	100	39	550	
	6	44	1.7				
3	0	45	2.2	133			Operation 9 hrs after injury First blood study within 24 hrs after injury Recovery
	1	65	2.3	142	44	530	
	2 A M	57	2.0	127	36	510	
	2 P M	67	2.0	125		540	
	3	73	2.0	133		525	
	4	42	1.5				
	5	34	1.4		47	530	
	6	30	1.4			610	
4	1	85.7	2.3	93		50	No operation Blood study within 12 hrs Death
5	7	100.0	4.5	125		400	No operation First blood study 7 days after injury Recovery Final blood studies 9 days after leaving the hospital
	8	93.8	5.2	105		390	
	9	100.0	4.5	95		390	
	10	100.0	6.2				
	11	79.0	4.5	118		450	
	12	86.0	3.0				
	13	60.0	3.5	102		560	
	14	60.0	3.2				
	15	60.0	3.5				
	16	58.0	2.5				
	17	49.2	2.1				
	18	54.0	2.0				
	27	26.0	1.5	62		495	

abdominal cavity contained a large quantity of blood. The round ligament was completely torn from the abdominal wall and there was a deep laceration far back into the inferior surface of the liver extending toward the hilum. Hemorrhage had almost ceased. There was some blood in the retroperitoneal tissues about the right kidney. The wound in the liver was packed with gauze. Following the operation the patient was quite ill for five days. Restlessness and delirium were sufficiently pronounced to require restraint. After the sixth postoperative day improvement was rapid. He made an uneventful recovery with the exception of a mild wound infection. The highest temperature during the first three days was 104.2° F.

The blood found in the urine on admission disappeared in two days, and granular casts were found at later examinations. Blood counts showed a leukocytosis and secondary anemia. There was a slight increase in the blood nonprotein nitrogen and creatinine the afternoon of the day of admission. In 24 hours after the injury the nonprotein nitrogen was 65 mg and the creatinine 2.3 mg per 100 cc of blood. The changes in the blood chemistry returned to normal in five days (Table I).

Case 4—P. H., male, age 10, was brought immediately to the hospital after having been injured by the wheel of a truck passing over his abdomen. He was in extreme shock. There were abrasions over the four lower ribs on the right and over the upper right lumbar area. The abdomen was rigid and tender. He was given a transfusion followed by infusion of dextrose in saline solution. The following morning his hemoglobin was 66 per cent and he was given another transfusion. Some dulness was noted in the flanks. A roentgenogram showed cloudiness at the base of both lungs. He vomited several times. A small quantity of blood was noted in the vomitus. Six hours after the injury he was quite irrational with a rising temperature which reached 104.2° F before death, 17 hours after the accident. Just before death he had a convulsion. The urine showed pus cells and hyaline and granular casts. Twelve hours after the injury the nonprotein nitrogen was 85 mg and the creatinine, 2.3 mg per 100 cc of blood (Table I).

At autopsy there were found a deep laceration in the dome of the right lobe of the liver, laceration of the spleen, blood in the abdominal cavity, retroperitoneal hemorrhage, pulmonary hemorrhage and edema and hemorrhage into the right adrenal. An area of liver tissue was macerated and grayish brown in color. Microscopic study of the liver showed diffuse necrosis of the injured portion with some inflammatory reaction. There was cloudy swelling of the kidneys and vacuolar hydropic changes in the cells of the convoluted tubules. The glomeruli were normal. There was some congestion of the stroma.

Case 5—A male, age 49, was admitted to St. Luke's Hospital, Kansas City, Missouri, June 22, 1936, on the service of Dr. E. L. Miller. He had been kicked over the liver by a man, seven days before admission. Pain in the abdomen was immediate and grew worse gradually until he called a physician on the seventh day, when he was sent to the hospital. His general appearance indicated dehydration. Examination revealed general abdominal tenderness which was more marked in the right upper quadrant. His hemoglobin on admission was 84 per cent and the following day was 81 per cent. Some abdominal distention had developed but no evidence of blood in the peritoneal cavity was demonstrated. Operation for ruptured liver was considered but because of his generally good condition this was deferred. With sedatives and parenteral liquids he showed gradual improvement and was discharged from the hospital in 12 days without operation. The highest temperature was 99° F. The urine showed albumin, occasional hyaline casts, and a few red blood cells and pus cells for six days following admission to the hospital. When he entered the hospital the nonprotein nitrogen was 100 mg and the creatinine 4.5 mg per 100 cc of blood. The changes in the blood chemistry persisted with slight increase in the creatinine to 6.2 mg for four days and gradually decreased to 5.4 mg of nonprotein nitrogen and 2 mg of creatinine the day of discharge from the hospital, 12 days after the accident. Twenty-one days after the injury the blood chemistry was normal (Table I).

Results of Experimentation—As soon as a relationship between liver injury and renal disease was noted, experiments were planned to reproduce the condition in animals. Helwig and Schutz attempted to traumatize the livers of dogs without breaking the liver capsule. They found it quite difficult to produce pulpefaction of the liver similar to that observed in patients. Dogs used for this work died quickly of shock after liver trauma. In dogs dying within 12 hours, they found an increase in the nitrogenous products of the blood and albumin, casts and red blood cells in the urine. The high levels in the blood nitrogen noted in clinical cases were not found. Animals living several days showed a progressive oliguria. Necropsy of animals dying within 12 hours showed parenchymatous degeneration of the more highly differentiated tubular epithelium of the kidneys and a marked hemorrhagic necrosis of the liver. They believed that their experimental results were sufficiently definite to substantiate the theory that some potent poison is elaborated by necrotic liver tissue which has a specific effect upon the kidney parenchyma. These authors were also able to demonstrate similar changes in the urine and blood after temporary ligation of the hepatic artery in rabbits. They have presented their clinical, pathologic, and experimental observations as a definite "liver-kidney syndrome."

Boyce and McFetridge attempted to reproduce the "hepatorenal syndrome" in animals by traumatizing the liver, and experienced the same difficulty as Helwig and Schutz. The changes found in the blood and urine confirmed the findings of the latter authors. Similar results were obtained by Pytel¹² in a series of experiments on 58 rabbits. He pointed out that there is a phylogenetic, anatomicophysiologic and pathologic relationship between the liver and kidneys. He concluded that injury and disturbance of liver circulation produced a symptom complex in animals analogous to the hepatorenal syndrome observed in man. Liver trauma was produced in a series of white rats and rabbits by Adler¹³. His animals developed oliguria and anuria. An increase in the rest nitrogen was observed in the rabbits. The kidney changes noted were cloudy swelling and vacuolization of the tubular epithelium. Fat droplets were demonstrable with sudan stain. Small groups of round cells were seen about dilated blood vessels. He was able to prevent the anuria and increase in rest nitrogen in rabbits by injecting "pehepar."

DISCUSSION—The relationship between liver and kidney damage incident to gall tract disease has been many times recognized in cases of suspected liver death following operations. It is probable that the same syndrome occurs in other diseases, especially those within the abdomen. In a recent (1939) review of the hepatorenal syndrome, Wilensky¹⁴ recognized a wide variety of hepatorenal symptoms and/or lesions including those due to chemical poisoning, abnormal physiologic states, infections, and disturbances of the ductless glands. A similar relationship exists between a traumatized liver and the kidneys. It has been generally believed that the liver, when severely injured by disease or trauma, produces a soluble toxin which causes definite pathologic changes in the kidneys. Boyce and McFetridge doubt the specificity of this

toxin but consider that the kidneys suffer in the fulfillment of the abnormal duty placed upon them. They recognize the possible direct effect of the toxin on the kidney tissue.

The five cases of liver trauma described here all manifested some degree of toxic effect upon the kidneys as shown by an increase in the blood of the non-protein nitrogen and creatinine and albumin, pus and casts in the urine. In the two cases examined at autopsy, changes similar to those already reported were observed in the liver and kidneys. It is interesting to note the rapidity with which the changes in the blood and urine occurred after severe liver injury. In less than 24 hours a retention of nitrogen was present and albumin, casts, frequently pus and erythrocytes appeared in the urine. Helwig and Schutz observed these rapid changes in the blood and urine of dogs dying within 12 hours after the liver was traumatized.

It is difficult to believe that infection is a factor in the liver and kidney changes. The three patients operated upon all had infected wounds, but the changes noted in the blood and urine were present before the infection developed. In Case 2, a general peritonitis was found at autopsy but the changes in the blood chemistry had returned to normal before death. It is believed that the cause of death in this patient was not due directly to the toxic effect of the liver trauma but to the complicating infection. In Case 1, the changes in the blood returned to normal although the patient developed a severely infected wound and later an empyema from which he recovered. In Klieg's¹⁵ analysis of 60 cases of hepatic trauma, he concluded that the evidence pointed to a toxic condition on an uninfected basis. Blood and urine studies were not reported by Klieg.

From the clinician's standpoint the practical value of the blood and urine findings incident to liver trauma are worthy of consideration. Although the nitrogen retention in the blood develops early following liver damage, the importance of early operation to control hemorrhage would negate the value of the changes in the blood and urine as a diagnostic aid in many cases. However, in those cases in which bleeding is slow and the condition of the patient warrants a few hours' delay to establish the diagnosis of liver injury, the changes in the blood and urine may be of some diagnostic value. In Case 2 of this series, operation was delayed 24 hours, during which time the nonprotein nitrogen rose to 131 mg and the creatinine to 4.1 mg per 100 cc of blood. This patient had other injuries complicating the picture, but knowing that such blood changes are associated with liver damage aided in confirming the diagnosis of liver rupture. Frequent estimations of the nonprotein nitrogen and creatinine may be of definite value in the prognosis. Certainly an increase in nitrogen retention indicates an increase in toxicity. Significant changes in the blood sugar, chlorides, or carbon dioxide combining power were not found. Delirium may be an outstanding symptom as observed in four of the patients reported. After a few days a hemorrhagic tendency develops similar to that observed in patients with jaundice.

In contrast to the above reports, Branch¹⁶ has recently described two

cases of severe liver injury, one of which lost approximately one-half of the liver and the other was closed after operation with a portion of necrotic liver remaining in the abdomen. Branch states that the urine and blood chemical studies in his first case were normal. Both of these patients recovered after operation. He concludes that a considerable portion of the liver must be destroyed before the so-called "liver-kidney" syndrome will appear.

The treatment of severe liver trauma is the treatment of shock plus operation to control bleeding and administration of dextrose to maintain liver glycogen and promote diuresis. The quantity of sodium chloride given must depend to some extent upon the quantity lost by vomiting. Usually the administration of chlorides is not an important factor in treatment.

CONCLUSIONS

All evidence presented, both clinical and experimental, leads to the conclusion that a traumatized liver may elaborate an unknown toxic substance which directly affects the kidneys producing both pathologic and functional changes.

The five cases here recorded emphasize the importance of careful blood chemical and urine studies. It is suggested that these studies are of definite prognostic value and in some cases may aid in the diagnosis of liver trauma.

These reports indicate that a consideration of the prognosis and treatment of liver trauma must not only include hemorrhage, shock, and complicating infection, but, in addition, a toxic factor produced by the damaged liver cells which directly affects the kidney parenchyma, causing an increase in the blood nonprotein nitrogen and creatinine, the appearance of albumin, casts, pus, and frequently red blood cells in the urine, and a decrease in the urinary output.

REFERENCES

- ¹ Helwig, F. C., and Orr, T. G. Traumatic Necrosis of the Liver with Extensive Retention of Creatinine and High Grade Nephrosis. *Arch Surg*, 24, 136, January, 1932.
- ² Helwig, F. C., and Schutz, C. B. A Liver Kidney Syndrome. *Surg, Gynec and Obstet*, 55, 570, November, 1932.
- ³ Schutz, C. B., Helwig, F. C., and Kuhn, H. P. Contribution to Study of So-Called Liver Death. *J A M A*, 99, 633, August 20, 1932.
- ⁴ Furtwaengler, A. Diffuse Rindennekrose beider Nieren nach Leberruptur. *Krankheitsforschung*, 4, 349, June, 1927.
- ⁵ Henschen, C. Die Bedeutung der Leber in der Chirurgie. *Arch f klin Chir*, 173, 488, 1932.
- ⁶ McKnight, R. B. Postoperative Physiological Studies in Case of Traumatic Rupture of the Liver, with Recovery. *Am Jour Surg*, 8, 542, March, 1930.
- ⁷ Stanton, E. McD. Immediate Causes of Death Following Operations on the Gallbladder and Ducts. *Am Jour Surg*, 8, 1026, May, 1930.
- ⁸ Rosenbaum, J. Ein Beitrag zum Problem des entero-hepato-renalen Syndroms. *Deutsch Ztschr f Chir*, 243, 66, 1934.

- ⁹ Helwig, F C, and Schutz, C B A Further Contribution to the Liver-Kidney Syndrome J Lab and Clin Med, 21, 264, December, 1935
- ¹⁰ Boyce, F F, and McFetridge, E M So-Called "Liver Death" Arch Surg, 31, 105, July, 1935
- ¹¹ Becker, F Schwere Nierenschädigung nach Leberruptur Zentralbl f Chir, 63, 674, March 21, 1936
- ¹² Pytel, A Zur Frage des Hepato-renalen Syndroms Arch f klin Chir, 187, 27 November, 1936
- ¹³ Adler, A Die Heilbarkeit des durch Leberruptur Entstandenen Schweren Nierenleidens in Tierexperimenten Zentralbl f Chir, 64, 142, January 16, 1937
- ¹⁴ Wilensky, A O Occurrence, Distribution and Pathogenesis of So-Called Liver Death and/or the Hepatorenal Syndrome Arch Surg, 38, 625, April, 1939
- ¹⁵ Krieg, E G Hepatic Trauma, Analysis of Sixty Cases Arch Surg, 32, 907, May, 1936
- ¹⁶ Branch, C D Injury of the Liver, Report of Two Cases ANNALS OF SURGERY, 107, 475, March, 1938

DISCUSSION —DR WARREN H COLE (Chicago) This is a very intriguing subject which Doctor Orr and Doctor Helwig have brought up, I have been much interested in it ever since their initial report, although, as Doctor Orr said, some of their points are controversial I have become convinced that the syndrome is a definite entity Part of their hypothesis is dependent upon the supposition that the devitalized liver tissue results in the formation of a toxic product acting directly on the kidney The complex nature of the chemical substances making up the liver, and the fact that we have plenty of evidence that on other occasions toxins may develop in tissue during the process of its degeneration or necrosis, are points supporting their hypothesis Moreover, we can all call to mind innumerable substances which, when given to animals, have a rather specific toxic action on the kidney

By analogy, I wish to offer further evidence supporting this traumatic hepatorenal syndrome by comparison with a patient who had the so-called hepatic insufficiency syndrome, but of the nontraumatic type This patient was a male, age 28, with Banti's disease, a very large spleen, jaundice, and ascites At operation, a splenectomy was performed The liver was found to be small and very badly scarred The operative course for three days was very satisfactory Then, on the fourth day, he began to become delirious and developed a fever, became nauseated, began to vomit, and a few days later coma developed During all this time there was marked leukocytosis At first the urine was negative, as it had been on entry, but after a few days, the N P N began to rise with a maximum of about 100, in the last few days albumin and blood appeared He died on the sixteenth postoperative day, autopsy was performed The microscopic section of the liver showed areas of necrosis of the liver cells This necrosis was spread throughout the entire liver section, and there was an entire disarrangement of the cellular pattern The microscopic section of the kidney showed a marked tubular degeneration with numerous hemorrhages throughout the kidney

Summarizing, the pathologic changes in the liver and kidney along with the progress of this patient show a marked similarity to the manifestations and pathologic findings in the traumatic cases described by Dr Orr If it is granted that the severe renal manifestations and pathologic changes seen in nontraumatic hepatic insufficiency of the type illustrated in the case just cited, are a part of a hepatorenal syndrome, it would appear just as logical to consider the renal changes in Doctor Orr and Doctor Helwig's traumatic cases likewise as a part of a hepatorenal syndrome

DR FREDERICK A COLLER (Ann Arbor, Mich) I am delighted that Doctor Orr has taken up a study of this hepatorenal syndrome, because up until the present I have remained very much unimpressed by those who have written on the subject. In fact, I have never been convinced that this entity exists. However, Doctor Orr has been right so many times that I am forced to reconsider and perhaps admit myself wrong.

There is no question about the facts. Of course, the only thing on which one might differ is an explanation of why they occur. Is there a toxin, or are there other causes that might explain this high nonprotein nitrogen and the changes in kidney and urine?

Formerly, we always blamed the kidney for all of these blood alterations that have been mentioned, but it is now known that there are many causes of extrarenal azotemia. There are at least five mechanisms that may well cause a rise in nonprotein nitrogen in the blood.

It has been shown that a drop in blood pressure will cause a marked diminution in the urine volume, which diminished directly with this fall in blood pressure until a systolic value of about 77 Mm. of mercury is reached. It is entirely conceivable that in states of surgical shock associated with disease or accident, this may play a part in diminishing urinary output and causing a nitrogen retention.

Hypochloremia and hyponatremia associated with vomiting, fistulae, diarrhea, ascites or shock may be associated with rise in blood proteins, although it has been suggested that sodium loss causes dehydration, which in turn will increase the concentration of the blood.

We rather commonly find high nonprotein nitrogen values from the blood associated with alkalosis due to pyloric obstruction and peritonitis. Dehydration will cause a concentration of the blood and all of its elements. Lashmet and Newburgh have shown that in normal conditions the kidneys excrete 35 to 40 Gm. of solids a day. This requires at least 500 to 600 cc. of urine for kidneys working at their maximal concentration. If the output is less than this, or if the kidneys have a decreased concentrating solution, there will be a nitrogen retention.

We carried out studies on healthy individuals who submitted to voluntary abstinence from water for several days, and it was found that there was a very definite rise in the nonprotein nitrogen of the blood caused by this mild type of dehydration. The urine showed very marked changes, the presence of albumin, increased casts, and red blood cells.

About three years ago, there were a number of papers published in which it was alleged that acute nephritis is frequently associated with acute cholecystitis. One observer reported eight cases with acute cholecystitis that died of acute nephritis. A typical history of one of these cases runs about as follows. A woman, admitted to the hospital in a typical attack of acute cholecystitis that had been present for three days. During this time she had not been able to eat or drink and had been vomiting. On admission to the hospital the patient was given half a liter of 50 per cent glucose and the following several days until her death, she was given about a liter of salt solution.

In comment, one may say that the patient entered the hospital dehydrated, was further dehydrated by the administration of hypertonic solution and was given inadequate fluids from then on. The urinary changes undoubtedly were entirely due to this drastic dehydration caused by disease and by treatment. This of course does not apply to the patients presented by Doctor

Or but I relate it to show that dehydration may well produce distinctly abnormal urine

Protein catabolism if increased is reflected by an increase in the urinary excretion of nitrogen. This occurs with large abscesses, septic inflammations such as pneumonia, peritonitis, septicemia, or even associated with severe surgical trauma. Damage to the liver itself, such as in cases of acute yellow atrophy, may cause a marked rise in the mono-acid nitrogen, and I am very inclined to believe that the damage to the liver in the cases presented by Doctor Orr may well play a part in producing the azotemia and abnormal urinary findings.

In short, it is my belief that while there may be a specific toxin generated by the injured liver that acts directly upon the kidneys, I think that in cases with liver damage we must remember that infection, fever, low blood pressure and dehydration may well be factors in causing nitrogen retention and in producing the urinary abnormalities that have been presented to us today, and certainly further studies, with these other factors in mind, must be made before we have definite proof of the existence of the hepatorenal syndrome as a clinical entity.

DR THOMAS G. ORR (closing). I have presented these cases as they are without any effort to explain the hepatorenal syndrome. I think that Doctor Coller would be the man to explain the mechanism of these changes in the liver and the kidney. A short time ago, Wilensky reviewed a large group of conditions which he thinks produce this so-called hepatorenal syndrome. I am not prepared to accept the condition wholesale, because there are so many other factors to be taken into consideration. Lastly, I am very happy that Doctor Coller now has become hepatorenal minded.

CONTROL OF POSTOPERATIVE BLEEDING IN OBSTRUCTIVE JAUNDICE*

J D STEWART, M D , G M ROURKE, B A ,

AND

A W ALLEN, M D

BOSTON, MASS

FROM THE SURGICAL LABORATORIES OF THE HARVARD MEDICAL SCHOOL AT THE MASSACHUSETTS GENERAL HOSPITAL,
BOSTON, MASS

MUCH convincing experimental and clinical evidence has been adduced during the past five years bearing on the mechanism of pathologic bleeding in obstructive jaundice^{1,2,3,4} Such bleeding has been shown to depend upon reduction in plasma prothrombin, which is probably part of the globulin fraction of plasma protein, formed by the liver. A fat-soluble substance, or substances, rather widely distributed in animal and vegetable fats and called vitamin K by Dam⁵ must be absorbed from the gastro-intestinal tract in the presence of bile salts for maintenance of normal prothrombin concentration. This metabolic process may be disturbed by factors depressing liver function, by lack of bile salts in the intestine, by insufficient intake of foods containing vitamin K, and probably by too rapid movement of the intestinal stream or too little absorptive intestinal mucosa. These considerations have a direct bearing on the control of the bleeding tendency in obstructive jaundice.

The data herewith presented were obtained in the management of cases of obstructive jaundice at the Massachusetts General Hospital during the past 12 months.

Methods Employed—These have been previously described⁶. The method of Warner, Binkhous and Smith, with modifications as described, has proved entirely satisfactory in the determination of plasma prothrombin. Measurement of plasma prothrombin, bilirubin and fibrinogen were made at frequent intervals before and after operation. The vitamin K extract used in this work was prepared from fresh spinach according to the method of Dam, and was mixed with sodium glycocholate and sodium taurocholate and put up in gelatin capsules containing 0.2 Gm. Each gram of the mixture was composed of 0.45 Gm. sodium glycocholate, 0.45 Gm. sodium taurocholate, and 0.1 Gm. of vitamin K extract derived from 200 Gm. of fresh spinach. The same lot of vitamin K-cholic acid mixture has been used throughout the work. In several instances a commercial preparation of vitamin K extracted from alfalfa (Klotogen, Abbott) has been used with satisfactory results.

Results Obtained—In Chart 1 appear data showing a dramatic improvement in prothrombin concentration and cessation of bleeding on administration

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

of vitamin K-cholic acid mixture in obstructive jaundice This patient had been operated upon a week previously and had not been given vitamin K When first studied there was massive bleeding from the wound, and the prothrombin concentration was extraordinarily low, 9.8 per cent Bleeding ceased and did not recur after vitamin K-cholic acid mixture was given the patient Blood transfusion was given three days later to restore hemoglobin values Plasma fibrinogen showed little change during the period of observation

Chart 2 shows prothrombin, fibrinogen and bilirubin values at various points in the management of a case of common duct obstruction from stone The prothrombin level rose rapidly to a normal figure on giving vitamin K-cholic acid mixture before operation The usual immediate postoperative drop took place, and the prothrombin concentration remained low until vitamin K-cholic acid mixture was given again, this time by jejunostomy The sharp postoperative elevation of plasma fibrinogen is of interest, and shows the lack of correlation between prothrombin and fibrinogen changes

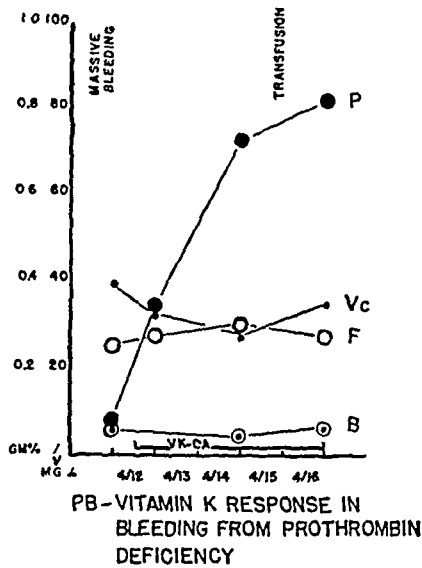
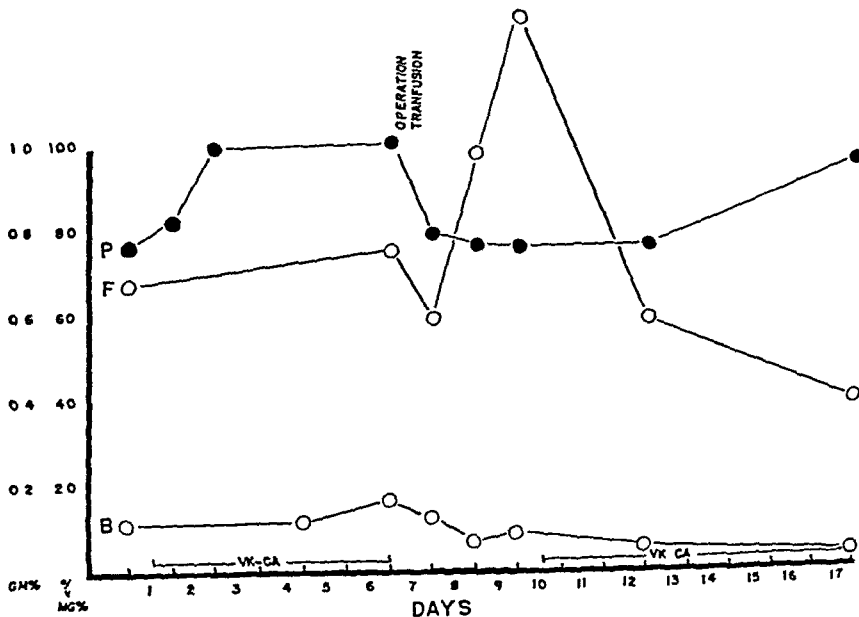


CHART 1—Case P B Vitamin K response in bleeding from prothrombin deficiency in obstructive jaundice P equals prothrombin concentration in per cent, Vc equals cell volume in per cent, F equals fibrinogen concentration in gm per cent, B equals plasma bilirubin concentration in mg per cent Vitamin K cholic acid mixture 1.2 gm per day given as shown



ELD- PLASMA PROTHROMBIN IN OBSTRUCTIVE JAUNDICE

CHART 2—Case ELD Plasma prothrombin in obstructive jaundice due to stone in the common duct Vitamin K cholic acid mixture 1.2 gm per day given by jejunostomy after operation P equals prothrombin concentration in per cent, F equals fibrinogen concentration in gm per cent, B equals plasma bilirubin concentration in mg per cent

In Chart 3 are shown observations over a period of eight weeks in a case of stricture of the common duct. At the first operation the common duct was drained, but internal flow of bile was not established, and nearly complete external biliary fistula resulted. Since the patient was taking the regular hospital diet fairly well five days after operation it seemed justifiable to study the effect on prothrombin concentration of giving cholic acid without vitamin K.

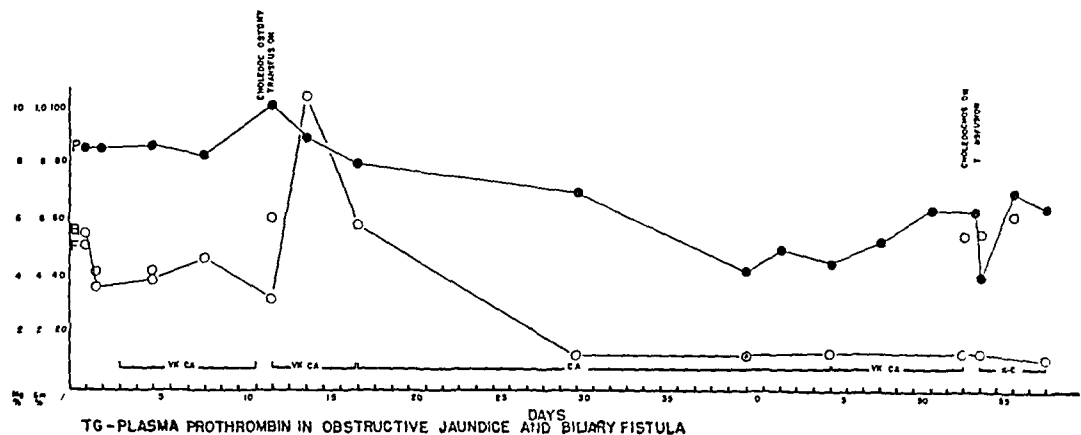


CHART 3—Case TG. Plasma prothrombin in obstructive jaundice and biliary fistula. VK CA indicates administration of 1.2 gm of vitamin K cholic acid mixture per day, CA indicates administration of 1.2 gm of bile salts per day. P equals plasma prothrombin in per cent, B equals plasma bilirubin in mg per cent, and F equals fibrinogen in gm per cent.

A gradual fall in prothrombin level resulted, and the low values persisted until vitamin K was again given the patient. Following the second operation the usual drop in prothrombin concentration with secondary response to vitamin K-cholic acid mixture is shown.

TABLE I

EFFECT OF OPERATION AND ANESTHESIA ON PLASMA PROTHROMBIN IN THE ABSENCE OF LIVER DISEASE. DETERMINATIONS IMMEDIATELY BEFORE AND AFTER OPERATION AND 24 HRS. LATER.

			Vc %	Fibrinogen Gm /100 cc	Plasma Protein Gm /100 cc	Plasma Pro- thrombin %
P R	Herniorrhaphy, spinal anes- thesia		49.2	0.26	7.02	95.0
			47.3	0.25	6.95	94.0
			54.1	0.41	8.06	91.0
L S	Hysterectomy, ether anes- thesia		45.3	0.28	7.88	100.0
			46.4	0.27	8.17	100.0
			44.7	0.40	7.98	100.0
E E	Hysterectomy, ether anes- thesia		40.7	0.27	7.54	90.0
			41.1	0.26	7.50	95.0
			40.5	0.40	7.23	98.0
I S	Hysterectomy, ether anes- thesia		47.6	0.62	8.30	85.0
			46.9	0.59	8.22	82.0
			39.7	0.65	7.25	70.0
A B	Abdominoperineal excision of rectum, spinal anesthesia		39.9	0.30	7.62	92.5
		*	41.7	0.13	7.27	87.2
		*	39.2	0.32	6.46	84.2

* Denotes transfusion 500 cc citrated blood

Table I shows data obtained in a study of changes in concentration of prothrombin, plasma protein, fibrinogen and red cell hematocrit in five patients subjected to extensive operations under ether or spinal anesthesia. The absence of significant changes in prothrombin values in patients without liver disease is to be contrasted with the observations in Table II. In Table III are shown cell volume values, plasma fibrinogen and prothrombin concentra-

TABLE II

EFFECT OF OPERATION AND ANESTHESIA ON PLASMA PROTHROMBIN, E. L. D. AND L. C. FOR COMMON DUCT STONE, T. G. FOR EXTERNAL BILIARY FISTULA, E. W. FOR CARCINOMA OF PANCREAS. T. G. AND L. C. NOT JAUNDICED. DETERMINATIONS IMMEDIATELY BEFORE AND AFTER OPERATION AND 24 HRS. LATER

Operation		Vc %	Fibrinogen Gm / 100 cc	Plasma Protein Gm / 100 cc	Plasma Prothrom- bin %	Plasma Bilirubin mg %
E. L. D.	Cholecystostomy,	35.1*	0.76	6.51	101.1	17.8
	choledochostomy	33.8	0.77	6.13	77.9	17.8
	jejunostomy-novocain	40.0	0.60	6.60	80.0	13.3
E. W.	Cholecystoduoden-	28.9*	0.79	6.31	91.9	8.6
	ostomy, jejunostomy-	26.5	0.52	5.12	92.9	7.2
	ether	33.8	0.60	6.13	77.6	6.6
T. G.	Choledochostomy,	37.9*	0.57	8.57	52.2	
	spinal-ether	40.0	0.53	8.32	65.8	
		41.3	0.58	7.63	41.6	
L. C.	Cholecystectomy	44.2	0.20	8.15	110.0	
	choledochostomy	45.1	0.27	7.76	97.6	
	ether	42.8	0.46	8.30	87.8	

* Denotes transfusion 500 cc citrated blood

TABLE III

EFFECT OF BLOOD TRANSFUSION ON PLASMA PROTHROMBIN DETERMINATIONS BEFORE AND AFTER TRANSFUSION OF 600 CC CITRATED BLOOD IN ADULT PATIENTS

Diagnosis		Vc %	Fibrinogen Gm / 100 cc	Prothrombin %
T. M.	Chronic osteomyelitis	33.1	0.74	53.2
		31.8	0.57	60.5
O. S.	Chronic lung abscess	35.9	0.53	61.1
		36.4	0.51	71.2
D. I.	Obstructive jaundice	42.4	0.78	77.4
		43.7	0.75	88.4

tions, immediately before and after transfusion of 600 cc citrated blood in adult patients. The increase in prothrombin values after transfusion in the three cases averages 9.5 per cent. In Tables IV and V are set down data illustrating the prothrombin response to vitamin K-cholic acid therapy before operation in obstructive jaundice due to stone and carcinoma. The maximal postoperative drop in prothrombin concentration in both groups of cases is tabulated with the time at which the drop occurred. The change in prothrom-

BLEEDING AND JAUNDICE

TABLE IV

PLASMA PROTHROMBIN RESPONSE TO VITAMIN K-CHOLIC ACID THERAPY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE DUE TO COMMON DUCT STONE BLOOD TRANSFUSION PERFORMED AT OPERATION IN EACH INSTANCE AVERAGE VALUES SHOWN BELOW CHANGES EXPRESSED IN ABSOLUTE PERCENTAGE VALUES

		Prothrombin						
		Duration Jaundice Weeks	Preoperative Response				Postop Drop	
Age Sex	Initial Value %		Change %	Duration Treatment Days	Vitamin K-Cholic Acid Gm	%	Day	
L H S	33-M	8	49 8	+37 0	4	3 2	-8 9	3
T G	46-M	Biliary fistula	43 6	+22 7	10	12 0	-24 7	1
D F W	39-M	2	35 7	+47 6	2	5 8	-45 6	3
M L K	61-F	8	70 7	+29 3	5	6 0	-57 9	9
E L D	70-F	2	77 8	+23 3	6	*	-24 2	2
R D	35-M	1	47 1	+43 2	2	1 8	-23 2	3
J M S	63-M	1 5	72 9	+19 7	5	6 0	-3 8	2
G K	71-F	4	81 3	+27 5	3	3 6	-15 3	1
J M S	34-F	0 5	95 0	+15 0	6	3 6	-39 1	4
R M	69-F	8	53 4	+51 7	4	**	-20 4	1
D P	22-F	1 5	68 6	+31 4	3	3 6	-15 7	2
Av		3 6	64 9	+31 7	4 5	5 1	-25 3	2 8

*Received daily 6,000 units vitamin K (Almquist-Stokstad) with bile salts

**Received daily 3,000 units with bile salts

TABLE V

PLASMA PROTHROMBIN RESPONSE TO VITAMIN K-CHOLIC ACID THERAPY IN PATIENTS WITH OBSTRUCTIVE JAUNDICE DUE TO CARCINOMA BLOOD TRANSFUSION PERFORMED AT OPERATION IN EACH INSTANCE AVERAGE VALUES SHOWN BELOW CHANGES EXPRESSED IN ABSOLUTE PERCENTAGE VALUES

		Prothrombin							
		Duration Jaundice Weeks	Preoperative Response				Postop %	Drop Day	
Age Sex	Initial Value %		Change %	Dura- tion Treat- ment Days	Vitamin K-Cholic Acid Gm				
J B	47-M	3	71 4	+15 2	5	4 0	-17 7	2	
H C K	32-F	4	71 1	+24 6	4	3 2	-25 0	4	
P W	58-M	5	28 9	+67 2	3	9 0	-30 4	7	
J R B	53-M	4	83 2	+16 8	6	24 3	-10 0	4	
T P H	66-M	6	28 0	+28 7	2	5 7	-18 6	4	
E W	73-F	8	23 1	+68 8	9	10 8	-14 3	1	
D N I	42-M	12	69 9	+ 9 3	4	5 2	-10 0	1	
W T M	54-M	4	67 6	+13 8	9	11 2	-29 5	4	
Av		5 8	55 4	+30 5	5 2	9 2	-19 4	3 4	

bin is expressed in absolute percentage and not percentage of the previous value. The amount of vitamin K-cholic acid mixture taken in each instance is recorded. The postoperative drop in plasma prothrombin occurred invariably in both groups of cases. In interpreting this finding allowance must be made for the fact that every patient had a blood transfusion at the end of the operation, which effects an immediate increase of from 6 to 10 per cent in prothrombin concentration.

Discussion—It is clear that plasma prothrombin concentration in obstructive jaundice is a labile quantity. The value rises rapidly under treatment with vitamin K-cholic acid mixture, and falls quickly under such depressing circumstances as infection, surgical operation, hemorrhage and anesthesia. This implies a lack of reserve prothrombin in obstructive jaundice and suggests the need for studying prothrombin concentration closely in managing these cases. In the more depleted patients we have performed jejunostomy at the time of operation on the biliary tract to avoid delay in the further administration of vitamin K-cholic acid mixture, as well as for feeding. This may occasionally be necessary in preparing a patient for operation on the biliary tract, particularly if veins are poor and the patient not thoroughly cooperative.

In connection with the immediate drop in prothrombin concentration after operation, an interesting question is the effect of the anesthetic agent. Evidence at hand suggests that the same depression of prothrombin level is seen after ether, spinal, or local novocain anesthesia, but the question needs further study. As seen in Table I, major surgical procedures in patients without liver disease may be performed under spinal or ether anesthesia without changes in prothrombin concentration. It is probable the patient with obstructive jaundice has depleted prothrombin reserves compared with the normal, and that the liver in obstructive jaundice is less resistant to depressing conditions.

In comparing the cases of obstructive jaundice due to stone with those due to carcinoma, it is apparent that the initial average prothrombin concentration is higher in the former group, the response to vitamin K-cholic acid therapy is more rapid, the dosage is smaller and the final preoperative prothrombin concentration is nearer normal. Hard and fast conclusions are hardly justifiable without further observations, but the data at hand suggest that the patients with carcinomatous obstruction have greater liver damage and are more likely to show pathologic bleeding. The danger from pathologic bleeding comes with prothrombin concentrations below 40 per cent, and the average preoperative and postoperative concentrations in these cases were well above this figure.

In considering the dosage of vitamin K-cholic acid mixture necessary to restore prothrombin concentration to a safe level, the extent of liver damage is of much importance. The data shown in Chart 3 are of interest in this connection. This patient had common duct stricture with a high degree of liver damage from biliary cirrhosis. After the first operation, which resulted in external biliary fistula, the patient was given cholic acid without vitamin K.

Despite the fact that the standard hospital diet was being taken fairly well the prothrombin concentration fell gradually, and the low values persisted until vitamin K was again given the patient. We have had the experience in other patients of failing to get a satisfactory response in plasma prothrombin until the dose of vitamin K-cholic acid preparation usually sufficient was doubled although in no case has failure to respond been complete. These have been patients with clinical signs of severe liver damage. These findings suggest the applicability of the law of mass action in this connection and indicate that the quantity of vitamin K given must be increased in the presence of factors hindering prothrombin formation.⁷

In treating prothrombin deficiency in obstructive jaundice the importance of measures which restore liver function, minimize liver damage, and favor renal function should be pointed out. A daily carbohydrate intake of 400 to 600 Gm, proper fluid therapy, and early decompression of the obstructed biliary tract are very helpful measures. In the desperately sick patient with complete biliary obstruction from carcinoma a two-stage operative plan is often desirable, the first operation being drainage of the distended gallbladder under novocain anesthesia after two to four days of preparation. Patients with obstructive jaundice have usually lost much weight and are in a state of general malnutrition. Cevitamic acid, vitamin B complex, and vitamins A and D should be given by mouth, or suitable preparations may be given parenterally. Finally, blood transfusion is often necessary as the most rapidly effective measure in dealing with reduction in hemoglobin and plasma protein. It has been our routine practice to give the patient a blood transfusion at the time of operation on the biliary tract.

CONCLUSIONS

(1) Plasma prothrombin concentration is reduced in obstructive jaundice, and may undergo a further drop immediately after operation.

(2) Prothrombin deficiency has invariably responded to proper vitamin K-cholic acid therapy, but larger doses and longer treatment were required in more severe grades of liver damage.

(3) The therapeutic importance of adequate intake of carbohydrate, proper fluids and other vitamins and of blood transfusion should be emphasized.

REFERENCES

- ¹ Almquist, H. J. Further Studies on the Antihemorrhagic Vitamin. *Jour Biol Chem*, **120**, 635, 1937.
- ² Hawkins, W. B., and Brinkhous, K. M. Prothrombin Deficiency the Cause of Bleeding in Bile Fistula Dogs. *Jour Exper Med*, **63**, 795, 1936.
- ³ Brinkhous, K. M., Smith, H. P., and Warner, E. D. Prothrombin Deficiency and the Bleeding Tendency in Obstructive Jaundice and in Biliary Fistula. Effect of Feeding Bile and Alfalfa (Vitamin K). *Am Jour Med Sci*, **196**, 50, 1938.
- ⁴ Snell, A. M., Butt, H. R., and Osterberg, A. E. Treatment of the Hemorrhagic Tendency in Jaundice with Special Reference to Vitamin K. *Am Jour Digest Dis and Nutrit*, **5**, 590, 1938.
- ⁵ Dam, H. The Antihemorrhagic Vitamin of the Chick. *Biochem Jour*, **29**, 1273, 1935.

- ⁶ Stewart, J D Prothrombin Deficiency and the Effect of Vitamin K in Obstructive Jaundice and Biliary Fistula ANNALS OF SURGERY, 109, 588, 1939
- ⁷ Snell, A M Vitamin K Its Properties, Distribution and Clinical Importance J A M A 112, 1457, 1939

DISCUSSION —DR ARTHUR W ALLEN (Boston) Any large general hospital might consider themselves fortunate to have a surgeon competent to make a study such as Doctor Stewart has just presented, not only sufficient chemical knowledge to follow these patients but also to make his own vitamin K It may not require a great deal of skill to boil down a hundred bushels of spinach in order to make this extract, but it is time-consuming

Also, the prothrombin level determinations that must be made on these patients, in order to follow them accurately, is a very heavy burden on his laboratory, and this brings up a point which I wish to stress As these new laboratory principles are evolved from the research department, and found essential in the routine care of patients, they must be taken over by the general laboratory and this creates an extra burden I had hoped that Doctor Stewart might be able to find a simple method of determining how much vitamin K and cholic acid might be required in a jaundiced patient and how many days of treatment were necessary without having to follow so closely the prothrombin levels Unfortunately, we have not been able, up to date, to formulate these requirements on a satisfactory basis other than by accurate laboratory data

The other point that I wish to bring up is a technical one I am quite sure in these very ill patients that it is wise to add a jejunostomy in order to be sure that you can continue to administer vitamin K and cholic acid immediately after operation Many of these patients will not be able to take the mixture by mouth for a few days and will have a very definite drop in prothrombin level Thus we may avoid a dangerous hemorrhagic stage and not be faced with emergency measures

THE SIGNIFICANCE OF THE CHOLESTEROL PARTITION OF THE BLOOD SERUM IN SURGERY OF THE GALLBLADDER¹

OTTO C PICKHARDT, M D , A BERNHARD, B S , A M , AND
IRVING L KOHN, M D

NEW YORK, N Y

FROM THE SURGICAL SERVICE AND THE ACHELIS LABORATORY, LENOX HILL HOSPITAL, NEW YORK, N Y

THE ADVENT of more accurate procedures for the estimation of cholesterol and its fractions in the blood serum has resulted in renewed interest in the rôle played by the liver in cholesterol metabolism. Any assumption that one can translate abnormal cholesterol findings into terms of liver function should be dismissed, since any one test has as yet failed to measure the many diverse functions of the liver. It is not within the scope of this paper to discuss the ever increasing accumulation of experimental data on the relationship between cholesterol metabolism and the liver, nor will any attempt be made to review the large amount of literature on liver function in general. There are, however, certain definite facts regarding the metabolism of cholesterol and its fractions, and their relationship to the liver which form the basis of our investigations and their clinical significance as reported in this paper. These are

(1) The concentration of the total cholesterol in the blood serum of each normal individual in health, is maintained at a constitutional level, which is characteristic for that individual, and is not subject to large deviations.^{1 2 3}

(2) There is a definite relationship between the amount of free and total cholesterol in normal persons. The percentage of free in total cholesterol appears to be a physiologic constant. The amount of free cholesterol in healthy adults varies between 24.3 and 30 per cent, with an average of 26.9 per cent of the total cholesterol.^{4,5}

(3) Changes in the ratio of free to total cholesterol are of considerably greater significance than changes in the concentration of total cholesterol, although, even in normal individuals there are wide variations, the concentration for the same individual, in health, is constant.

It is generally believed that esterification of cholesterol esters from cholesterol and the higher fatty acids is accomplished by the liver.^{6 7} The liver also has the ability through cholesterol esterases to hydrolyze cholesterol esters. The maintenance of this reversible reaction is a normal physiologic process of the liver, which, we believe, can be measured by the determination of the cholesterol partition of the blood serum.

As stated above, in normal individuals the ratio of esterified to free cholesterol is a physiologic constant. Any alteration in this relationship, *etc.*, a rise

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

in the percentage of free cholesterol, with a corresponding decrease in ester cholesterol, regardless of the amount of total cholesterol, indicates a disturbance in the ability of the liver to regulate the synthesis and hydrolysis of cholesterol esters, a disturbance which has been explained by Thannhauser and Schaber⁸ on the basis of damage to the hepatic cells

We believe that the liver has a functional reserve, which is reflected by changes in the cholesterol partition. A rise in the percentage of free cholesterol of the blood serum is indicative of a lowering of the functional reserve. This would be analogous to the CO₂ combining power of the blood plasma as a measure of the alkaline reserve in acidosis. Therefore, throughout this paper we will refer to changes in the per cent of free cholesterol as a measure of the functional reserve of the liver. We propose to show that the demonstration of changes in the cholesterol partition is of clinical value in determining the functional reserve of the liver in hepatic disturbances, associated with surgery of the biliary tract, and, as such, serves to indicate the optimum time for a planned surgical intervention.

Procedures—The technical methods employed for the determination of total cholesterol were those described by Bernhard and Dreker,⁹ Dreker, Bernhard and Leopold,¹⁰ and Bernhard.¹¹ Free cholesterol was determined by the modification of the Schoenheimer and Speiry technique described by Dreker, Sobel and Natelson.¹² Ester cholesterol determinations were made on the supernatant fluid and washings, after precipitation of the free cholesterol, by evaporation to dryness, extraction with petroleum ether, again evaporated and dried, and the residue taken up with chloroform and the cholesterol determined as in total cholesterol. The icterus index was determined by the method described by Bernhard and Maue, cited by Stetten.¹³ In all our investigations the blood was obtained before breakfast, the serum separated and the determinations made as soon as possible. Serum was used, because Speiry and Schoenheimer¹⁴ have shown that oxalated plasma contains significantly smaller amounts of total and free cholesterol than either serum or heparinized plasma from the same sample of blood.

Normal Values—With our technical methods, our own normal figures in 51 healthy adults were as follows. Total cholesterol varied between 141 and 404 mg per 100 cc of serum. Free cholesterol varied between 31 and 110 mg per 100 cc of serum. The per cent of free cholesterol varied between 16 and 30, with an average of 23 per cent. These figures compare with those reported by Speiry.⁴

Clinical Material—We have classified our cases into three groups

(A) Cases of acute and chronic cholecystitis and cholelithiasis in which operation was performed and in which the cholesterol partition was within normal limits

(B) Patients operated upon showing a high percentage of free cholesterol

(C) Nonoperated cases showing an increased percentage of free cholesterol

Group A—Cases of acute and chronic cholecystitis and cholelithiasis in

which operation was performed and in which the cholesterol partition was within normal limits indicating a normal functional reserve of the liver (Table I)

This group also included four patients who showed an initial decreased functional reserve as revealed by the increase in the percentage of free cholesterol. These four patients received the usual medical treatment including a low fat, high carbohydrate diet, with additional forced glucose ingestion. Under this regimen there was an improvement in the functional reserve as shown by a drop to normal values in the percentage of free cholesterol. In

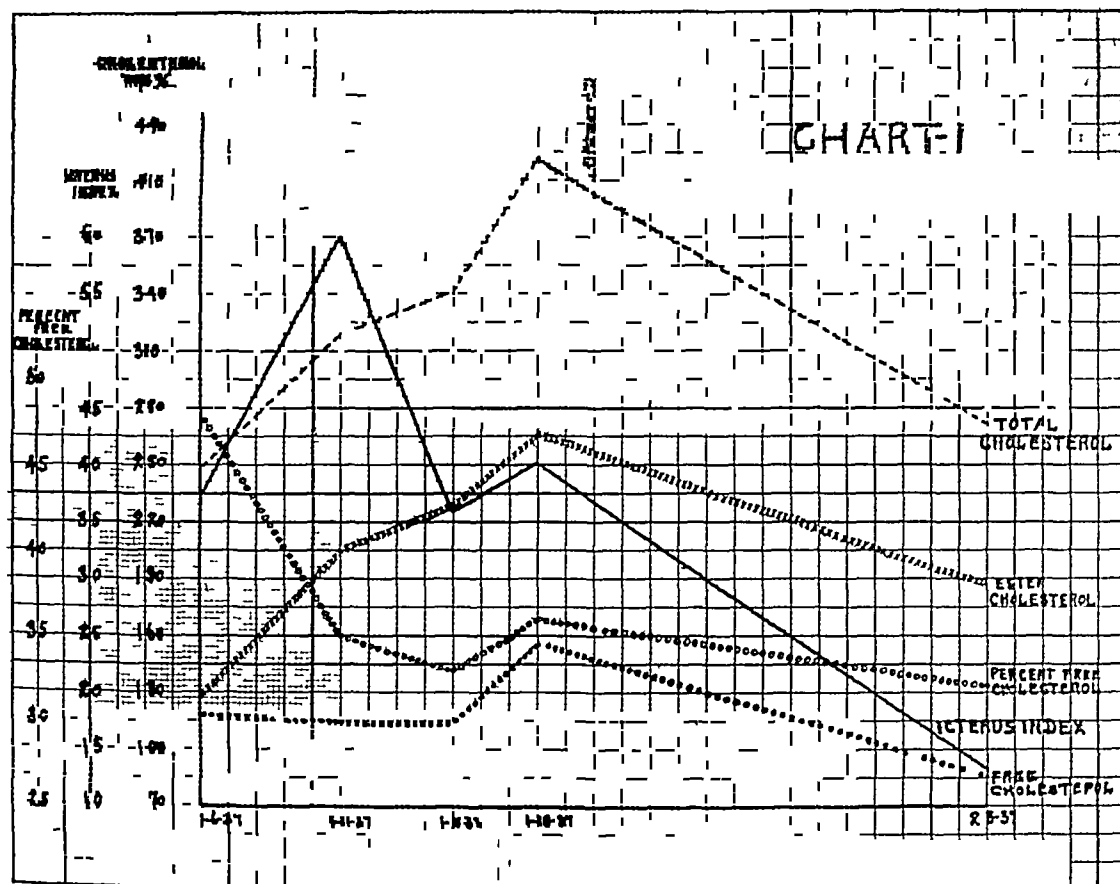


CHART I—Case 1 Hosp No 55835 Chronic cholecystitis and cholelithiasis with initial diminished functional reserve, which returned to normal preoperatively after medical treatment. Good postoperative course.

these patients operation was delayed until the functional reserve was restored. A typical case (Case 1 No 55835) is graphically illustrated in Chart I.

Case 1—Hosp No 55835. A white female, age 46, complained of sharp pain in the right upper quadrant, and jaundice of ten days' duration, with clay-colored stools and dark urine. There were two previous attacks, similar in nature, 5 and 11 months before the present attack. Her temperature, pulse and respiration were normal. Examination of the abdomen revealed tenderness in the right upper quadrant and a palpable mass two fingers' breadth below the right costal border. The pertinent laboratory findings were Wassermann negative, icterus index 37, total cholesterol was 246, ester 128, and the free cholesterol 118 mg (48 per cent). A diagnosis of chronic cholecystitis and cholelithiasis was made. The patient was placed upon the routine medical treatment because the cholesterol partition revealed a low functional reserve of the liver. The cholesterol

TABLE I
CASES OPERATED UPON IN WHICH THE CHOLESTEROL PARTITION WAS WITHIN NORMAL LIMITS

Hist No	Age	Sex	Date	Icterus Index	Serum Cholesterol Mgs Per 100 Cc			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
49058	50	F	6-19-36	42	220	140	80	36	Acute cholecystitis and cholelithiasis Operation 6-23-36—Cholecystectomy
55452	34	F	12- 8-36	47	240	160	80	33	Chronic cholecystitis and cholelithiasis Operation 12-14-36—Cholecystectomy
			12-12-36	14	181	125	56	30	
			12-28-36	8 3	226	166	60	26	
45420	45	F	2- 5-37	21 4	254	174	80	31	Chronic cholecystitis and cholelithiasis Operation 2-8-37—Cholecystectomy
39365	45	M	2-18-37	11	245	161	84	34	Chronic cholecystitis and cholelithiasis Operation 2-19-37—Cholecystectomy embolus—Death
27811	57	F	6-16-37	57	232	160	72	31	Chronic cholecystitis and cholelithiasis Operation. 7-12-37—Cholecystectomy Stones in common duct
			6-25-37	22	205	135	75	36	
37820	66	F	10- 9-37	60	275	195	80	28	Acute cholecystitis and stone in common duct
			10-18-37	19	268	188	80	29	Operation 10-25-37—Cholecystectomy and choledochotomy
60150	32	F	10-20-37	25	232	172	60	26	Chronic cholecystitis and cholelithiasis
			10-27-37	10	212	156	56	26	Operation 10-28-37—Cholecystectomy
61273	59	M	12-15-37	50	209	145	64	30	Chronic cholecystitis and cholelithiasis
			12-20-37	20	288	223	66	23	Operation 1-11-38—Cholecystectomy

THE CHOLESTEROL PARTITION

66264	59	F	2-17-38	6	6	280	200	80	28	Chronic cholecystitis and cholelithiasis Operation 2-21-38—Cholecystectomy
54347	47	M	2-18-38	7	5	256	196	60	23	Chronic cholecystitis and cholelithiasis Operation 2-21-38—Cholecystectomy
61251	36	M	1-21-38	25		185	133	52	28	Fistula of common duct Operation 3-16-38—Revision and implantation of common duct into duodenum
52439	44	M	2-7-38	40		206	152	54	26	Previous operation 12-18-37—Cholecystectomy
55835	46	F	2-14-38	33		150	106	44	29	Acute cholecystitis and cholelithiasis Operation 5-29-36—Cholecystectomy
			2-24-38	62	5	183	123	60	32	Chronic cholecystitis and cholelithiasis Preoperative treatment
			2-28-38	44		146	98	48	33	Operation 1-20-37—Cholecystectomy
			5-23-36	120		212	102	100	47	Preoperative treatment
			5-27-36	33		216	146	72	33	Chronic cholecystitis and cholelithiasis Preoperative treatment
			1-6-37	37		246	128	118	48	Operation 1-20-37—Cholecystectomy
			1-11-37	60		319	205	114	35	Preoperative treatment
			1-15-37	36		342	228	114	33	Chronic cholecystitis and cholelithiasis
			1-18-37	40		421	266	155	36	Stone in common
			2-3-37	13	3	271	184	87	32	Preoperative treatment
			10-29-38	51		355	195	160	45	Chronic cholecystitis and stones in cystic and common ducts
			11-2-38	72		353	213	140	39	Preoperative treatment
			11-22-38	22		297	228	69	23	Chronic cholecystitis and cholelithiasis
			11-1-38	93		346	118	228	66	Operation 11-30-38—Cholecystectomy
			11-12-38	70		548	320	228	42	Stone in common
			11-16-38	60		394	266	266	32	Preoperative treatment
66220	48	F								Drainage of com-

examinations were repeated five days later, and showed a decrease in the percentage of free cholesterol to 35 per cent although there was a rise of the icterus index to 60. The same treatment was continued and four days later there was a decrease in the free cholesterol to 33 per cent and a marked drop in the icterus index to 36. Examinations made three days later showed about the same values for the cholesterol partition, and it was thought that this was the opportune time to operate since improvement in the functional reserve was so evident.

At operation a gallbladder filled with stones was found, as well as a stone in the common duct. Cholecystectomy and removal of the common duct stone were done. The patient made an uneventful recovery. Two weeks after operation the cholesterol partition was determined, and the free cholesterol was 32 per cent.

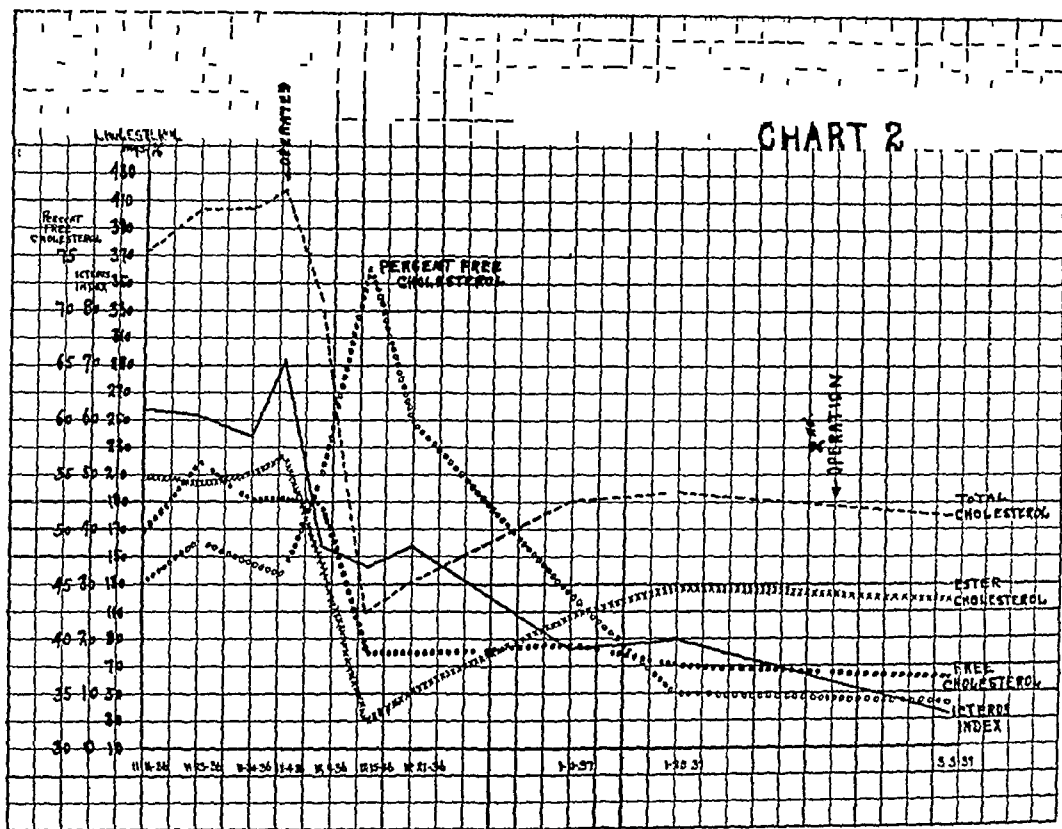


CHART 2—Case 2 Hosp No 55111 Chronic cholecystitis with decreased functional reserve—not improved by medical treatment. The percentage of free cholesterol was increased at time of operation. Stormy postoperative course.

COMMENT—This case and the other three similar cases in this group showed at the time of admission that there was a lowered functional reserve of the liver as demonstrated by the increase of the percentage of free cholesterol in the serum. After preoperative therapy, improvement in the reserve was reflected by decrease in the free cholesterol per cent, and when this value returned to normal it was believed that the patient was in better condition to withstand surgical intervention.

All the other patients comprising this group in which the percentage of free cholesterol was normal, indicating good functional reserve of the liver, had a smooth postoperative course.

Group B—Patients operated upon showing a high percentage of free cholesterol (Table II).

TABLE II

CASES OPERATED UPON WHICH SHOWED A HIGH PERCENTAGE OF ILL CHOLESTEROL AT TIME OF OPERATION

Hist No	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg Per 100 Cc			Choles- terol	Per Cent Free	Diagnosis and Remarks
					Total	Ester	Free			
55111	43	F	11-16-36	62	373	208	168	45		Chronic cholecystitis
			11-23-36	61	404	204	200	49		Operation 12-4-36—Cholecystectomy and drainage of com- mon duct
			11-30-36	57	405	213	192	47		No stones found, but common duct markedly dilated
			12-4-36	71	417	225	192	46		Operation 2-15-37—Cholechohorraphy
			12-9-36	37	337	149	188	55		
			12-15-36	33	108	28	80	74		
			12-21-36	37	132	52	80	60		
			1-11-37	18	191	107	84	44		
			1-25-37	20	198	128	70	35		
			3-3-37	6	180	118	62	34		
56175	62	F	1-27-37	125	286	113	173	60		Carcinoma of gallbladder with metastases to liver
			2-9-37	143	230	70	160	70		Operation 2-1-37—Celiotomy
			2-18-37	140	228	42	186	81		
			6-10-37	62 5	218	118	100	45		
58381	50	F	6-16-37	53	222	136	86	39		Chronic cholecystitis and cholelithiasis
			6-22-37	71	163	87	76	46		Operation 6-18-37—Cholecystectomy and drainage of com- mon duct 7-4-37—Expired Necropsy—Hepatitis
			6-12-36	174	132	70	62	46		Syphilis of the liver Complete obstruction of common duct
			10-9-36	44	439	276	163	37		Operation 2-28-36 Liver drainage
P11152	42	M	10-31-36	89	494	204	290	58		Operation 11-28-36 Hepatoduodenostomy
			11-10-36	222	258	70	188	73		
			11-18-36	133	360	160	200	55		
			12-10-36	47	214	100	114	53		
			12-26-36	31	186	110	76	40		
										1-9-37—Expired

This group consists of four cases in which the percentage of free cholesterol was definitely increased. The course of Case 2, Hosp No 55111, typical of this group, is shown graphically in Chart II.

Case 2—Hosp No 55111. A white female, age 43, was admitted, November 14, 1936, complaining of increasing jaundice and intermittent epigastric pain, radiating to the back, of four weeks' duration. The stools were clay-colored, urine very dark brown. There was occasional nausea but no vomiting. Patient had been treated for syphilis 17 years before, and at that time had also been jaundiced. Temperature, pulse and respiration were normal. Examination of the abdomen revealed generalized tenderness, most marked in the epigastrium and right upper quadrant. The icterus index was 62, total cholesterol 373, ester 208, free cholesterol 168 (45 per cent). Feces showed presence of bile. The Wassermann and Kline tests were both negative. A special Graham series, the dye being administered over a period of four days, showed no definite pathology. Due to the fact that the initial percentage of free cholesterol was increased, showing a lowered functional reserve of the liver, it was decided to place the patient under routine medical treatment. During the next two weeks, the percentage of free cholesterol increased slightly, being 49 and 47 per cent, and the icterus index 61 and 57 respectively. The patient during this period showed neither clinical nor functional reserve improvement. On December 3, 1936, 20 days after admission, patient had severe attacks of right upper quadrant pain, and it was thought she might have a stone in the common duct. Operation was advised. Icterus index rose to 71 on the following day, and the percentage of free cholesterol remained approximately the same (46 per cent) still indicating poor functional reserve.

At operation December 14, 1936, a chronically inflamed gallbladder was found, and the common bile duct was dilated, but no stones were found. Cholecystectomy and drainage of the common duct were performed. Nothing abnormal was felt in the pancreas. The postoperative course was extremely stormy from the very onset, with a rise of temperature to 104° and 105° F, pulse 120, and respiration 22 for the first three days. Intravenous therapy of saline and glucose was given almost continuously. Five days postoperative, the icterus index fell to 37, but there was a definite rise in the percentage of free cholesterol to 55 per cent. The spiking temperature continued, and then several hemorrhages from the wound occurred which were controlled after transfusions. Ten days postoperative, there was a sharp drop in the total cholesterol to 108 mg, with a marked rise in the free cholesterol percentage to 74 per cent. Icterus index was 33. The course continued to be stormy, and one week later the total cholesterol began to rise while the percentage of free cholesterol had decreased to 60 per cent. The patient began to improve gradually. About one month after operation, the stools again became clay-colored and there was profuse bile drainage from the wound (the T-tube had been removed on the seventeenth postoperative day). The icterus index on January 11 was 18, and the percentage of free cholesterol was 44, showing a definite improvement in the functional reserve of the liver. Two weeks later there was continued clinical improvement, and on January 25 the free cholesterol was 35 per cent, indicating further recovery in the functional reserve. Because of the biliary fistula, a second operation was considered and it was thought that due to the improved functional reserve, surgical intervention would be well tolerated at this time.

Accordingly, a secondary reconstruction of the common bile duct was performed, February 15, 1937. The postoperative course was entirely different from that following the original operation. There was only a slight rise in temperature which quickly returned to normal, and the patient made an otherwise uneventful recovery. A follow-up of this patient, March 3, 1937, showed that the icterus index was normal, being 6, and the percentage of free cholesterol was 34. On December 9, 1937, an exploratory operation was performed upon this patient at another hospital, because of recurring symptoms. A primary carcinoma of the pancreas with metastases to the liver was found, and the patient expired December 21, 1937.

COMMENT—In this patient, the initial determination of the cholesterol partition of the blood serum revealed a high value for the percentage of free cholesterol, indicating a decreased functional reserve of the liver. It will be observed that up to the time of the first operation there was a slow but definite rise in the percentage of free cholesterol. It will also be noticed that after operation the patient developed fever with a marked drop in the concentration of total cholesterol. In spite of this continued increase in temperature, the total cholesterol began to rise and the free cholesterol percentage had started to fall which is quite in keeping with McQuarrie's and Stoesser's¹⁵ observation that there is no constant relationship between the height of fever and degree of hypocholesterolemia. As the free cholesterol percentage continued to fall, indicating improvement in the functional reserve, there was also a marked clinical improvement in the condition of the patient. There was almost a normal percentage at the time of the second operation. The fact that the patient's second postoperative course was uneventful, we assumed to be on the basis of a marked improvement in the functional reserve. This case illustrates the value of frequent determinations of the cholesterol partition as a guide in prognosis.

Case 3—Hosp No P56175. A white female, age 62, was admitted, January 26, 1937, complaining of epigastric distress and painless jaundice of one month's duration. The stools were light yellow in color, and the urine was dark. Examination of the abdomen revealed slight tenderness in the right upper quadrant, and the liver was palpable two fingers' breadth below the right costal border. Temperature, pulse and respiration were normal. Important laboratory findings were Icterus index 125, total cholesterol 286 mg, ester 113 and the free cholesterol 123 mg (60 per cent), indicating a lowered functional reserve. A plain film of the abdomen revealed a shadow which was interpreted as a stone in the fundus of the gallbladder. Preoperative medical treatment was not instituted.

At operation, January 31, 1937, five days after admission, an inoperable carcinoma of the gallbladder with metastases to the liver and pancreas was found. The postoperative course was poor, the icterus index rising to 143 and the free cholesterol to 70 per cent. One week later, the icterus index was 140 with a further rise in the percentage of free cholesterol to 81 per cent. The patient's clinical condition became gradually worse, and she expired six weeks later.

COMMENT—From the very onset, the examination of the serum of this patient revealed a marked increase in the percentage of free cholesterol showing diminished functional reserve which, postoperatively, became progressively worse.

Case 4—Hosp No 58381. A white female, age 50, was admitted, June 10, 1937, complaining of three attacks of upper abdominal pain radiating to the back. The first attack occurred one and a half years before admission. The present attack was accompanied by nausea, vomiting and jaundice of four days' duration. Temperature, pulse and respiration were normal. There was moderate tenderness in the right upper quadrant of the abdomen, and a small rounded mass was thought to be felt just below the right costal margin. Laboratory examinations revealed a negative Wassermann, icterus index was 62.5, total cholesterol was 218 mg, ester 181 mg and free cholesterol 100 mg (45 per cent), showing a diminished functional reserve. A roentgenogram of the abdomen revealed several calcified shadows which were thought to be faceted gallstones. The patient

was placed on medical regimen for a week, at which time the icterus index was 53 and the percentage of free cholesterol was 39

At operation, June 18, 1937, a small contracted gallbladder containing a stone, and two stones in the common duct were found. Cholecystectomy and drainage of the common duct was performed. Postoperatively, this patient did not do well. The jaundice increased and the temperature was elevated. Four days postoperative, there was marked nausea and vomiting and the icterus index was 71, the percentage of free cholesterol being 46. The patient was given almost continuous intravenous infusions of saline and glucose. During the following days, there was a sanguineous discharge from the wound. Transfusion was given. She continued to bleed intermittently for the next few days and her condition became very poor. She expired two weeks after operation. Postmortem examination was performed and a diffuse hepatitis with necrosis of the liver cells was found.

COMMENT—This patient also showed a poor preoperative functional reserve without postoperative improvement, associated with a stormy postoperative course and death.

Case 5—Hosp No P11152. A white male, age 42, was admitted, February 20, 1936, with a history of increasing jaundice and general abdominal pains, chills and fever for the past six weeks. There was a past history of intestinal amebic infection and treated syphilis. Laboratory findings showed an absence of bile in the stool, an icterus index of 100, Wassermann 4+ and Kline 4+. Examination of the abdomen revealed a greatly enlarged liver with its edge extending eight centimeters below the costal margin. The edge was sharp and not tender. The spleen was moderately enlarged. There were no paraumbilical dilatations of the superficial veins. Roentgenologic examination showed no evidence of stones but a markedly enlarged liver.

An exploratory operation, February 28, 1936, revealed an enlarged, congested liver, a thickened gallbladder containing no bile or stones, a completely fibrosed and nonpatent common duct, and an exceedingly hard, constricting mass at the junction of the right and left hepatic ducts in the liver. This contained mucopurulent material which, on immediate examination, showed no ameba. The head of the pancreas was enlarged and hard. A piece of the liver was excised for further examination and because no drainage could be instituted into the common duct, two large tubes were inserted into the liver itself in the region of the hepatic ducts.

The patient had a very stormy postoperative convalescence but began to improve after the fifth day when bile appeared through the drainage tube. The pathologic report was syphilitic granuloma of the peritoneum, small gumma of the liver with acute and chronic hepatitis and bile stasis. The patient gradually improved with occasional remissions, care being taken to keep the drainage tubes open and bile escaping to the surface. His jaundice disappeared, but at no time was there any bile in the stool. Fresh pig's bile was fed him daily. He left the hospital 14 weeks later for further convalescence at which time the cholesterol partition showed a free cholesterol of 46 per cent.

He returned to the hospital, October 6, 1936, with a history of lessening bile drainage, increasing jaundice, fever and chills, loss of weight and general malaise. Antisyphilitic treatment was continued. In view of the general course of the disease, it was decided to attempt an anastomosis between the liver and the duodenum. At this time, as shown in Table II, the percentage of free cholesterol was 37. On October 31, the icterus index was 89 and the free cholesterol 58 per cent, showing further decrease in functional reserve, and in addition the permanent biliary fistula was markedly contracted. On November 10, there was a decided increase both in the percentage of free cholesterol and icterus index. The former was 73 and the latter 222.

The second operation was performed November 28, 1936, and the same pathologic conditions as previously observed were again found. An anastomosis between the right lobe of the liver and the duodenum was performed, and two large drainage tubes also placed directly into the liver. Pathologic examination of the removed tissue was reported

as chronic hepatitis (biliary cirrhosis), no evidence of malignancy. The patient again had a very stormy convalescence followed by a period of improvement as soon as bile drainage became established. The anastomosis held for several weeks with the appearance of bile in the stool, and then a duodenal fistula appeared. During the next three weeks, the percentage of free cholesterol remained elevated, but there was a drop in the icterus index. These values remained practically unchanged, until fatal termination of the disease, January 9, 1937.

COMMENT—This case was apparently one of syphilis of the liver with increasing fibrosis causing complete biliary obstruction. There was evidence

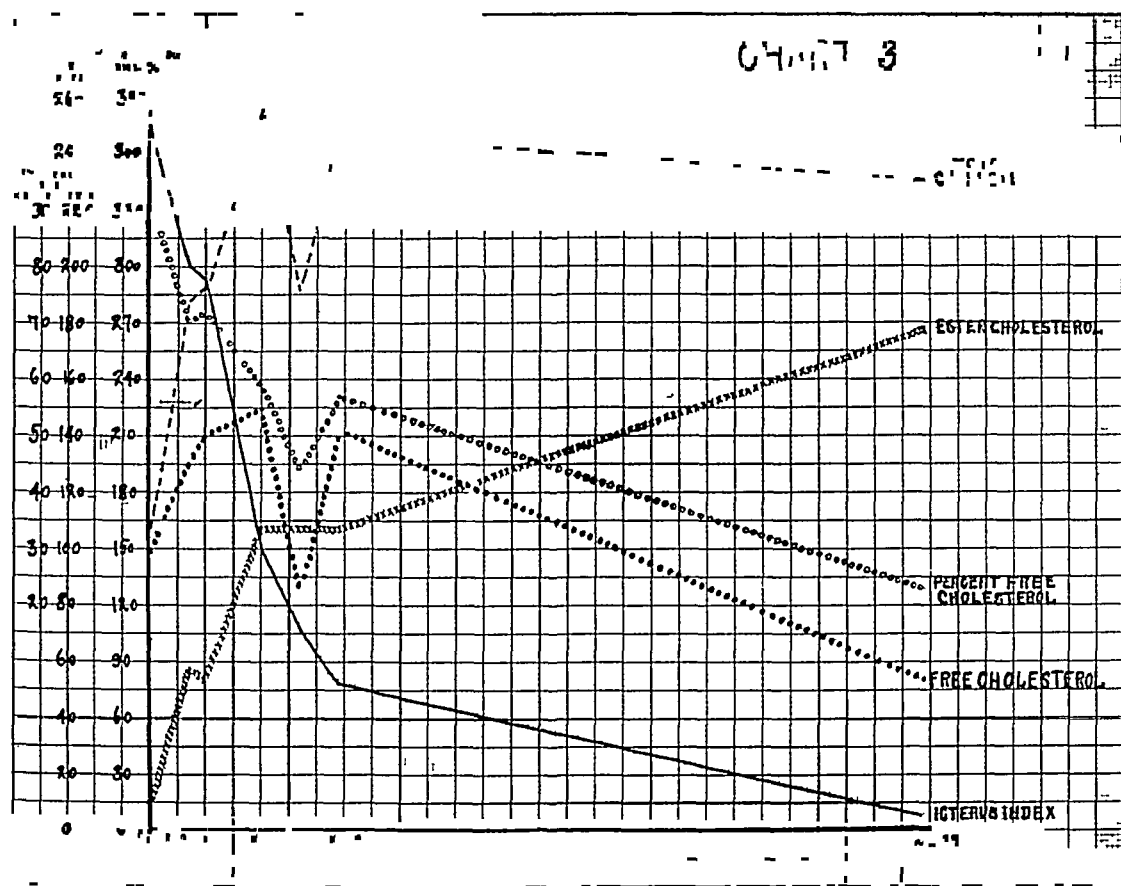


CHART 3—Case 6 Hosp No 65549 Catarrhal jaundice Nonoperated case Very high per centage of free cholesterol on admission which gradually returned to normal under medical treatment Case illustrates the prognostic value of the cholesterol partition

of poor functional reserve with no improvement during the postoperative course, indicating a poor prognosis

Group C—Nonoperated cases showing an increased percentage of free cholesterol (Table III)

This group consists of eight cases of catarrhal jaundice studied over a period of time, three cases of portal cirrhosis, one case of cholecystitis and cholelithiasis, and one case of gangrenous cholecystitis. Detailed observations of Case 6, Hosp No 65549 are shown graphically in Chart III, and this case will be discussed in order to show the value of the cholesterol partition in a patient with a questionable surgical diagnosis

Case 6—Hosp No 65549 A white male, age 57, was admitted, September 20, 1938, complaining of painless jaundice of four weeks' duration. There was anorexia and loss

TABLE III
CASES NOT OPERATED UPON WHICH SHOWED AN INCREASED PERCENTAGE OF FREE CHOLESTEROL

Hist No	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg Per 100 Cc			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
52139	34	M	5-7-36	227	213	109	104	49	Catarrhal jaundice
			5-11-36	133	211	108	103	48	
			5-15-36	71 5	216	128	86	40	
			5-26-36	29	205	131	74	36	
			6-2-36	22	257	177	80	30	
			6-26-36	10	169	112	57	33	
52802	33	M	6-9-36	143	205	95	110	54	Catarrhal jaundice
			6-16-36	142	164	50	114	69	
			6-22-36	142	222	106	116	57	
			6-30-36	142	230	106	124	54	
			10-10-36	172	225	62	163	72	
			10-16-36	165	178	30	148	80	
54588	47	M	10-24-36	100	173	39	134	77	Catarrhal jaundice
			10-29-36	77	274	128	146	56	
			11-10-36	37 5	214	114	100	46	
			11-17-36	28	208	130	78	37	
			11-23-36	20	185	116	69	37	
			10-16-36	104	242	94	148	61	
54691	38	F	10-22-36	80	254	80	174	68	Catarrhal jaundice
			10-28-36	35	204	122	82	40	
			11-4-36	31	192	116	76	40	
			10-21-36	49	197	111	86	43	
			10-26-36	23	253	119	134	53	
			10-31-36	20	194	122	72	37	
54753	65	F	11-11-36	14	152	114	38	25	Acute cholecystitis and cholelithiasis 10-24-36—Patient passed gallstone

THE CHOLESTEROL PARTITION

[illegible]

TABLE III (Continued)

Hist No	Age	Sex	Date	Icterus Index	Serum Cholesterol Mg Per 100 Cc			Per Cent Free Choles- terol	Diagnosis and Remarks
					Total	Ester	Free		
65549	57	M	9-21-38	250	160	12	148	92	Catarrhal jaundice
			9-28-38	201	281	85	196	70	
			10- 1-38	195	290	80	210	72	
			10-10-38	100	384	160	224	59	
			10-17-38	71	286	160	126	44	
			10-24-38	52	373	160	213	57	
66041	42	F	2- 6-39	6	346	266	80	23	Portal cirrhosis
			10-27-38	34	381	163	218	56	
			11- 7-38	25	528	266	266	49	
			11-14-38	40	700	424	276	39	
			11-27-38	18	794	552	242	30	
			12- 2-38	11	633	457	176	27	
66947	26	M	12-20-38	12	593	393	200	33	Catarrhal jaundice
			12-28-38	10	434	310	124	28	
			12-21-38	110	213	50	160	76	
			12-28-38	99	232	72	160	68	
			1- 4-39	40	222	142	80	36	
			1-12-39	28	212	160	52	24	

of 20 pounds in weight. Examination of the abdomen showed the liver to be palpable two fingers' breadth below the right costal border. There was no tenderness or rigidity. Temperature, pulse and respiration were normal. Important laboratory findings were Wassermann negative, urea nitrogen 41.5, normal blood count, icterus index 250, total cholesterol 160 mg, ester 12 mg, free cholesterol 148 mg (92 per cent), showing almost a complete absence of ester cholesterol. Bile was present in the feces. A Graham series showed a faint gallbladder shadow which was regular in outline. After a fatty meal, there was a complete disappearance of the gallbladder shadow. Patient was given routine medical treatment and a week later the icterus index dropped to 201, there was also a drop in the free cholesterol to 70 per cent, showing an improvement in the functional reserve. Four days later, the icterus index was 190 with practically no change in the cholesterol partition. Ten days later, there was a very marked drop in the icterus index to 100 and a marked decrease in the free cholesterol percentage to 59, showing further improvement both clinically and in the functional reserve. A week later, the icterus index was 71 and the percentage of free cholesterol 44. The patient left the hospital October 17, and returned a week later for follow-up, at which time the icterus index was 52, free cholesterol 57 per cent. Four months later, an examination showed that the icterus index was 6, free cholesterol 25 per cent, showing complete restoration of a normal functional reserve. At that time the urea nitrogen was 20.

COMMENT—The question as to whether this was a medical or surgical jaundice was not definite on admission. Because of the very high percentage of free cholesterol and poor functional reserve, it was decided not to perform an exploratory operation but to treat the patient medically. Marked clinical improvement in this patient proceeded in the same ratio as improvement in the functional reserve as shown by the decreasing percentages of free cholesterol. This case illustrates very well the value of repeatedly determining the functional reserve. It should also be noted that decrease in percentages of free cholesterol is a good prognostic sign.

Case 7—Hosp. No. 55612. A white female, age seven, was admitted to the hospital, October 19, 1937. Twice within an interval of three months, the patient had had symptoms of painless jaundice and pruritus. Examination of the abdomen revealed slight tenderness over the right upper quadrant and an enlargement of the liver five centimeters below right costal border. Stools were clay-colored, icterus index 25, total cholesterol 540 mg, ester 280, and free cholesterol 260 mg (48 per cent), indicating a decreased functional reserve. Roentgenograms of the gallbladder showed no evidence of stones. She was extremely ill, and temperature ranged between 102° and 105° F. During the next month, the percentage of free cholesterol varied between 40 and 62, and the icterus index rose to 83. On November 20, there was a definite drop in the percentage of free cholesterol to 33, remaining at that level for a period of ten days, with the icterus index at 36. There was also an improvement in the clinical condition of the patient during this time. Immediately following the period of normal functional reserve just mentioned, the percentage of free cholesterol progressively increased reaching a high of 73, and clinically the patient became worse. This figure ranged between 53 and 60 per cent until fatal termination of the disease. The icterus index also rose, reaching a high of 143 on December 20, and decreased to 62 at the time of death. At autopsy, a perforated gangrenous gallbladder was found. A stone was found lying free in the abdominal cavity. There was a generalized peritonitis and the liver was studded with numerous small abscesses.

COMMENT—Again, this case illustrates the value of the cholesterol partition as a guide to surgical intervention. If surgical intervention was to be

attempted in the case, the time to have operated would have been when the free cholesterol percentage had dropped to practically normal values, remaining so for about ten days. The prognostic value of the test is illustrated by our observations of this patient. The continued rise in the percentage of free cholesterol following the short period of normal functional reserve, is reflected by the poor clinical course and fatal termination.

In all of the other cases in this group, it will be noted that the initial value of the free cholesterol percentage was generally much higher than those in the other groups. After these patients had received medical treatment, it was observed that they improved, as shown by the progressive decrease in the percentage of free cholesterol. This indicated a recovery period, with improvement in the functional reserve. Accompanying this there was also a definite decrease in the icterus index. We stress the value of repeated determinations of the cholesterol partition as a prognostic aid in following the course in these patients.

Discussion—It is generally accepted that disturbances of hepatic function may be reflected by changes in the cholesterol partition of the blood. Early observation of this fact was reported by Feigl,¹⁶ who noted low ester cholesterol values in acute yellow atrophy. Thannhauser and Schaber⁸ were quick to recognize and emphasize the significance of this observation. They found the ester fraction to be greatly diminished, and the free cholesterol increased in cases of severe parenchymatous hepatic diseases, and attributed this phenomenon, which they named "*Esterstunz*," to a disturbance of cholesterol ester synthesis, and hydrolysis in the liver. Recently, Boyd and Connell¹⁷ have indicated that lipopenia is associated with the cholesterol "*Esterstunz*" in parenchymatous hepatic disease.

Opposed to the view of Thannhauser and Schaber⁸ is that of Gardner and Gainsborough,¹⁸ who state that diminution in ester cholesterol is due to impaired absorption of cholesterol and fat from the intestine in the absence of bile. Hawkins and Wright¹⁹ were unable to substantiate this explanation since they have shown that the absence of bile in the intestines and faulty fat absorption in dogs with biliary fistula did not result in changes of ester to total cholesterol ratio.

Clinical evidence for and against the interpretation of the above stated opinions have been reviewed by Gardner and Gainsborough,¹⁸ Epstein,²⁰ Epstein and Greenspan,²¹ and Shay and Fieman.²² Most of the investigators have tried to translate changes in the cholesterol partition into terms of liver function. It was thought to be of value in differential diagnosis between obstructive and nonobstructive jaundice. However, the general impression is that in uncomplicated parenchymatous hepatic disease, there usually occurs a diminished ester cholesterol value with a corresponding increase in the percentage of free cholesterol.

As stated by Boyd and Connell,¹⁷ "the original explanation of Thannhauser and Schaber is the most reasonable one to account for the changes in cholesterol partition when damage to the hepatic cells has occurred. Cholesterol

esters are not stored to any extent in normal tissues, although they are apparently synthesized as a by-product in degenerating tissue. A lessened production of cholesterol esters would thus soon result in a diminution in their concentration in the blood, the only medium in which they are found to any extent. Thannhauser and Schaber⁸ have argued that since damage to the liver lowers the cholesterol fraction in the blood, it is likely that these substances are produced in the liver. Supporting this is the fact that cholesterol esterases have been found in the liver."

Previous investigators, reporting on the estimation of the cholesterol partition, have utilized methods which we believe are not so accurate as those of recent origin. By the newer procedures the free cholesterol in normal individuals generally is not greater than 30 per cent of the total cholesterol as against variations of 30 to 50 per cent, which were formerly considered as normal. Refinement in technical procedures has resulted in better evaluation of the observations thus obtained and in better clinical interpretation.

We have utilized the changes in the cholesterol partition of the blood serum as a measure of the functional reserve of the liver and have presented evidence to show that this interpretation is of value to the surgeon. This value lies in an indication as to the most opportune time for surgical intervention in disease involving the gallbladder and biliary tract. This fact is amply demonstrated by the data given in Table I. Actually, all of these patients, with the exception of No. 39365, who died of a pulmonary embolism, did well postoperatively. Further evidence that the functional reserve plays a rôle in the ability of the patient to withstand operation, is shown by the four cases in which the initial functional reserve was diminished, and who received medical preoperative treatment, which resulted in restoration of this reserve. We are of the opinion that if these patients had been operated upon during the period of decreased functional reserve, their postoperative course would have been poor.

Further, patients operated upon in whom the cholesterol partition revealed a lowered functional reserve, as shown by observations recorded in Table II, all had a stormy postoperative course. Several terminated fatally. The third patient of the group, No. 55111, underwent two operations, previous to and during the first postoperative period, this patient had a low functional reserve as shown by the increased percentage of free cholesterol. With improvement in the reserve there was also marked improvement in the clinical condition. At the time the second biliary tract operation was performed, her functional reserve was considered normal, and the postoperative course, in contrast with the previous one, was uneventful. This particular case illustrates that the information obtained from the determination of the cholesterol partition is of definite prognostic value.

CONCLUSIONS

Determination of the cholesterol partition of the blood serum, particularly the changes in the percentage of free cholesterol, has been used as a measure of the functional reserve of the liver.

A patient who exhibits a low functional reserve of the liver is a poor operative risk. Medical treatment should be instituted, and repeated estimations of the cholesterol partition will indicate when the functional reserve has returned to normal. Such information is of value as a guide to surgical intervention.

The cholesterol partition has prognostic value in surgery of the gallbladder and biliary tract.

We suggest that the cholesterol partition of the blood serum be determined both pre- and postoperatively in all patients with biliary disease and jaundice.

REFERENCES

- ¹ Sperry, W. M. The Concentration of Total Cholesterol in Blood Serum. *Jour Biol Chem*, **117**, 391, 1937.
- ² Turner, K. B., and Steiner, A. A Long Term Study of the Variation of Serum Cholesterol in Man. *Jour Clin Invest*, **45**, 18, 1938.
- ³ Boyd, E. M. Diurnal Variations in Plasma Lipids. *Jour Biol Chem*, **110**, 61, 1935.
- ⁴ Sperry, W. M. The Relationship Between Total and Free Cholesterol in Human Blood Serum. *Jour Biol Chem*, **114**, 125, 1936.
- ⁵ Smith, R. M., and Marble, A. The Colorimetric Determination of Free and Combined Cholesterol. *Jour Biol Chem*, **117**, 673, 1937.
- ⁶ Wilder, R. M., and Wilbur, D. L. Diseases of Metabolism and Nutrition. *Arch Int Med*, **61**, 297, 1938.
- ⁷ Dalton, A. J. Cholesterol Storage and Bile Secretion in Chorio-Allantoic Grafts of the Liver. *Anat Record*, **67**, 431, 1937.
- ⁸ Thannhauser, S. J., and Schaber, H. Über die Beziehungen des Gleichgewichtes Cholesterin und Cholesterinester im Blut und Serum zur Leberfunktion. *Klin Wchnschr*, **5**, 252, 1926.
- ⁹ Bernhard, A., and Dreker, I. J. A Simple and Accurate Method for the Determination of Cholesterol in Blood Serum and Plasma. *Jour Lab and Clin Med*, **16**, 1225, 1931.
- ¹⁰ Dreker, I. J., Bernhard, A., and Leopold, J. S. The Extraction of Cholesterol from Blood Serum. *Jour Biol Chem*, **110**, 541, 1935.
- ¹¹ Bernhard, A. A Simple and Efficient Reflux Condenser. *Jour Lab and Clin Med*, **19**, 314, 1933.
- ¹² Dreker, I. J., Sobel, A. E., and Natelson, S. Fractionation of Cholesterol in Blood by Precipitation as Pyridine Cholesteryl Sulphate and Cholesterol Digitonide. *Jour Biol Chem*, **115**, 391, 1936.
- ¹³ Stetten, D. The Surgical Value of the Estimation of the Bile Pigmentation (Icterus Index) of the Blood Serum. *ANNALS OF SURGERY*, **76**, 191, 1922.
- ¹⁴ Sperry, W. M., and Schoenheimer, R. A Comparison of Serum, Heparinized Plasma, and Oxalated Plasma in Regard to Cholesterol Content. *Jour Biol Chem*, **110**, 655, 1935.
- ¹⁵ McQuarrie, I., and Stoesser, A. V. Influence of Acute Infection and of Artificial Fever on Plasma Lipoids. *Proc Soc Exper Biol and Med*, **29**, 1281, 1931.
- ¹⁶ Feigl, J. Über das Vorkommen und die Verteilung von Fetten und Lipoiden im menschlichen Blutplasma bei Ikterus und Cholestasie. *Chemische Beiträge zur Kenntnis spezifischer Lipamien*. III. *Biochem Ztschr*, **90**, 1, 1918.
- ¹⁷ Boyd, E. M., and Connell, W. F. Lipopenia Associated with Cholesterol Estersturz in Parenchymatous Hepatic Disease. *Arch Int Med*, **61**, 755, 1938.
- ¹⁸ Gardner, J. A., and Gansborough, H. Blood Cholesterol Studies in Biliary and Hepatic Disease. *Quart Jour Med*, **23**, 465, 1930.
- ¹⁹ Hawkins, W. B., and Wright, A. Blood Plasma Cholesterol Fluctuations Due to Liver Injury and Bile Duct Obstruction. *Jour Exper Med*, **59**, 427, 1934.

- ²⁰ Epstein, E Z The Cholesterol Partition of the Blood Plasma in Parenchymatous Diseases of the Liver Arch Int Med, 47, 82, 1931
Idem Cholesterol of the Blood Plasma in Hepatic and Biliary Diseases Arch Int Med, 50, 203, 1932
- ²¹ Epstein, E Z, and Greenspan, E B Clinical Significance of the Cholesterol Partition of the Blood Plasma in Hepatic and in Biliary Diseases Arch Int Med, 58, 860, 1936
- ²² Shay, H, and Fieman, P The Value of a Combined Study of the Newer Laboratory Test in the Differential Diagnosis of Toxic and Obstructive Jaundice Including Blood Phosphatase, Cholesterol, Galactose Tolerance and Glucose Tolerance Am Jour Digest Dis and Nutrit, 5, 597, 1938-1939

Discussion—DR JOHN A WOLFER (Chicago) The subject presented by Doctor Pickhardt is one that I have been interested in for some time, and I think all of you have been interested in the matter of the liver as a very essential factor in biliary tract surgery The physiologists tell us that, so far as they know now, the liver may have approximately 22 functions and probably there may be a few zeros added to that in the course of time Therefore, it is extremely interesting, and probably pertinent, to realize that there is no one function test of the liver As to whether isolated portions of the liver or specific liver cells perform certain functions there is a question I am inclined to feel that there is a considerable overlapping of liver anatomy with liver function

I should like to present three charts which will indicate the value of establishing the blood cholesterol partition, to see how it compares with conditions as we meet them

CHART I

F K, male, age 55 Entered hospital August 29, 1938
Pain in the abdomen and jaundice of 8 days' duration Clay-colored stools
Mass in the right upper abdomen which varied in size Loss of weight
Operated upon September 9, 1938, cholecystduodenostomy
Diagnosis Carcinoma of the head of the pancreas with liver metastases
Autopsy October 20, 1938 Diagnosis verified 4000 Gm of carcinoma in the liver

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict Ind	Ser Bil	N P N	B U N
	Total	Ester	Free	%	Total	Alb	Glob					
8-30-38	255	140	115	45	6.8	4.4	2.4	109	91	11.7	34.5	15.7
9-1-38	251	133	118	45					93	12.1		
9-9-38					Cholecystduodenostomy							
9-12-38	186	97	89	48	6.3	3.38	2.92		50	5.9	28.3	12.0
9-16-38	180	109	71	33	6.3	3.37	2.93		40	2.6		13.4
9-23-38	207	140	67	32	6.3	3.38	2.92		25	1.0	27.3	12.3
9-30-38	205	138	67	32	6.5	3.34	3.16		20	1.0		
10-10-38	177	104	73	41	6.9	3.38	3.52		17			
10-14-38	152	86	43	43	7.0	3.42	3.58		17			
10-20-38					Expired							

Chart I is from the study of a male, who had pain in the right abdomen, jaundice for eight days' duration, clay-colored stools, and a mass in the right upper abdomen which fluctuated in size from time to time There was a loss of weight He was operated upon and a carcinoma of the head of the pancreas was found with metastases in the liver A cholecystduodenostomy was performed September 9, 1938 The man died in October and the diagnosis was verified, there being found approximately 4,000 Gm of carcinoma in the liver Here we have a case with a high grade biliary obstruction which was relieved by operation with a residue of extensive carcinoma of the liver You

will note that the original cholesterol study revealed 45 per cent free cholesterol and normal plasma proteins. We are studying the plasma protein albumin-globulin ratio as a parallel with the cholesterol partition, on the assumption that esterification of cholesterol and the formation of protein fractions occur in the liver. The blood sugar was normal, the icterus index 91 and 92, serum bilirubin 11 and 12, and the blood urea nitrogen and nonprotein nitrogen not elevated. Following operation, there was an immediate rise in the free cholesterol to 48 per cent, but after a few days there was a distinct fall to 32 per cent. During this time there was a marked drop in the icterus index and serum bilirubin, as was to be expected. Due to drainage, however, a little later, ten days before death, the percentage of free cholesterol again began to increase. It is also interesting to note that during the terminal two weeks there appeared an inversion of the albumin-globulin ratio of the plasma protein—albumin 3.42 and globulin 3.58. Also, there is shown that the icterus index has fallen to 17 and the serum bilirubin to 1.0. In my opinion this chart clearly demonstrates and verifies Doctor Pickhardt's theory. The high percentage of free cholesterol was the result of liver damage. There was some

CHART II

L. G., male, age 52, February 3, 1939

For 3 weeks malaise, anorexia and abdominal discomfort. Jaundice for 4 days.

Highly colored urine for 10 days. Long history of sinus infection. Jaundice deepened with marked itching of the skin. Some low grade fever. Low blood pressure.

Diagnosis: Diffuse hepatitis with cirrhosis. Ascending cholangitis.

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict Ind	Serum Bil	N P N	B U N	Proth Time	Ser Phos
	Total	Ester	Free	%	Total	Alb	Glob							
2-4-39									200					
2-11-39									210				50.8	
2-17-39									250				40.5	
2-22-39	278	645	213.5	77.8									35.7	
2-24-39									250				34.8	
2-28-39	157	387	148.3	79.3	5.53	3.68	1.85					12.9	32.9	
3-2-39														
Drainage of Gallbladder														
3-6-39									150	40.2		9.3	32.4	
3-17-39	238	174	64.0	26.9	6.05	4.14	1.94		50	4.5	30.6	13.3		7.0
3-18-39														
Tube Out														
4-11-39	281	195	86.0	30.3	6.80	4.59	2.21	86	50	1.0	39.4	18.2		3.3

immediate relief by drainage, as expressed by a decrease in free cholesterol, however, because of the extensive liver damage due to carcinoma the relief was only temporary, to be followed by increasing percentages of free cholesterol and inversion of the albumin-globulin ratio of the plasma proteins.

Chart II is from the study of a male, age 52. There was a history of approximately three weeks of increasing weakness, anorexia and abdominal discomfort. Jaundice appeared about four days before admission to hospital, and itching of the skin, which had been present for some days, became progressively worse. The first cholesterol study revealed 77 per cent free, and a few days later it had risen to 79.3 per cent. The icterus index on first study was 200 and rose to 240 and finally to 250. The prothrombin time, based upon a standard of 20 seconds as normal, was 50.8 seconds. In spite of active treatment with large amounts of viosterol and calcium, a high sugar intake with vitamin K and bile salts, the symptoms became more acute. The prothrombin time had dropped to 32.9 seconds, however, but the percentage of free cholesterol had risen to 79.3 per cent as previously mentioned. He was operated upon two days after the last mentioned blood chemistry work. At exploration, the liver was found to be hard, retracted and mottled. The ducts were

not dilated but were gray in color and the walls thickened. Because of the poor reaction of the patient, a solitary small stone was removed from the gallbladder and the viscus was drained. The contents consisted of a clear yellow fluid. It will be noted that after an uneventful postoperative course of approximately two weeks, the free cholesterol had dropped to 26.9 per cent, which can be considered normal, the icterus index to 50 units, and, 40 days after operation, the free cholesterol was 30.3 per cent, and the serum bilirubin 1.0. In this instance, the clinical improvement of the patient closely paralleled the improvement or return to normal of the percentage of free cholesterol.

CHART III

G. K., male, age 46, March 10, 1939

In March, 1938, noted jaundice, pain in right side of abdomen, and weakness. Occasional vomiting. In July, 1938, reported at Clinic. Marked jaundice and loss of weight. Large abdominal tumor believed to be liver. Wassermann positive.

Diagnosis: Malignant disease. Put on antilutetic treatment and improved very materially but liver did not decrease in size. Explored March 15, 1939.

Diagnosis: Extensive amyloid disease of the liver.

Date	Cholesterol				Plasma Protein			Blood Sugar	Ict Ind	Serum Bil	N P N	B U N	Proth Time	Ser Phos
	Total	Ester	Free	%	Total	Alb	Glob							
3-13-39	334	180	153	46	6.59	4.01	2.58	80.4	30	1.5	29.5	12.5	32.75	47.78
3-14-39			60% clearance—Hippuric Acid											
3-15-39			Exploration—Biopsy from Liver											
3-17-39					7.60	4.75	2.40			4.5			81.85	
3-24-39													30.35	
3-28-39	248	103.5	144.5	58	5.86	3.74	2.12	79.5	55	6.5	21.7	9.55	22.00	23.08
4-7-39	212	97.5	114.5	54	5.40	3.16	2.24		30	2.3	44.2	27.8	$\left. \begin{array}{l} 24.00 \\ 29.2 \\ 19.1 \end{array} \right\}$	33.5
4-21-39	368	96.0	272.0	74	7.60	4.50	3.10	82.0	50	2.72	27.3	12.0		137.0
4-26-39	417	122.0	295.0	71	7.40	4.55	2.85	86.6	40	1.5	30.0	12.5		94.0
4-27-39			69.4% Clearance—Hippuric Acid											

The observations shown in Chart III were made on a case of proven extensive amyloid disease of the liver. Preoperatively, the free blood cholesterol was 46 per cent, there was a normal albumin-globulin ratio of the blood plasma protein, the prothrombin time was 32.75 seconds, and the serum phosphatase was 47.7 units. The hippuric acid test showed 60 per cent clearance. The operation consisted of an exploration with removal of a small piece of the liver for microscopic study. Two days after operation, the prothrombin time was 81.85 seconds (normal 21 seconds), he began bleeding from the wound, there was evidence of subcutaneous hemorrhage and his condition became critical. He was given "klotogen" and bile salts through a duodenal tube, and because of severe dyspnea, oxygen was administered. A week later, the prothrombin time had fallen to 30 seconds and bleeding had practically ceased. Two weeks after the exploration, the free cholesterol was 58 per cent and the serum phosphatase 23 units. It will be noted that 37 days after operation the free cholesterol was 74 per cent, the albumin-globulin ratio practically normal, the icterus index 50, the prothrombin time 19 seconds, and the serum phosphatase 137 units. At this time, he was feeling quite well. However, it is quite evident that he has extensive liver crippling because of the diffuse amyloid disease, and this is demonstrated by an increasing free cholesterol and serum phosphatase. Nevertheless, one function of his liver had adjusted itself—that which deals with blood clotting as evidenced by a normal prothrombin time and cessation of bleeding.

I feel, as does Doctor Pickhardt, that in the study of blood cholesterol partition we have at our disposal one test which will aid us in formulating an

opinion relative to the condition of the liver, and will act as one guide as to when surgical interference may be carried out with relative safety

DR ROBERT L. PAYNE (Norfolk, Va.) This presentation by Doctor Pickhardt seems to me to corroborate what we have observed over a period of about five or six years now and followed in our biliary surgery, namely, Epstein's work, which practically correlates the presentation he has made to-day, that is, the high total cholesterol and the low esters

I noticed in all of the charts, of both Doctor Pickhardt and Doctor Wolfer, that in those cases that showed a marked liver dysfunction, the cholesterol were high and the esters low, and that is the point Epstein so ably brought out and emphasized in numerous articles

As Doctor Wolfer aptly said, there are too many functions to the liver for any one liver test to be of great value, but I think if one is getting any help out of anything that he is doing, he at least ought to express it, and we have been getting a great deal of comfort for about three or four years now out of determinations of xanthoprotein and blood indican in suspected and determined liver dysfunction. This is based on the fact that physiologists tell us that the indol group is broken up in the liver through a mechanism in which ether sulphuric acid breaks up the indol into xanthoprotein and indican. Where this mechanism is disturbed, this does not take place, and in the blood you find an increase of xanthoprotein and a lowering of blood indican, which is just exactly the reverse of an Epstein lipid nephrosis in which the xanthoprotein is increased and the blood indican is increased

In those gallbladder cases where we have drained the common duct or where there is a biliary fistula, we have, in addition, been getting a great deal of comfort out of the study of the chlorides of the bile excreted

We have noted that where there is an impending liver dysfunction the bile chlorides will rise and with an improvement in the liver condition the chlorides will fall. Correspondingly, with this bile study we have carried Epstein's work out on the total cholesterol and the esters and we have found that although Epstein prognosticates the definite improvement when the ester relationship to the totals approach normal, yet it is a slower process than the determination of the chlorides in the bile. In other words, we make out in a daily chemical examination of the bile that a falling chloride, approaching normal, will indicate a return of the liver to its normal function two or three days sooner than the cholesterol estimations according to the Epstein method

DR OTTO C. PICKHARDT (closing) I did not know that Doctor Wolfer was working on this problem until he wrote me about it, and I was much interested to hear that his results were very much in line with ours

This test does not indicate the type of liver damage, that is, one can get a low functional reserve in such various conditions as Cholelithiasis, carcinoma, catarrhal jaundice, hepatitis and chronic passive congestion. Therefore, we do not want it thought that we have used this test for a differential diagnosis—we have not!

Doctor Payne's remarks on Epstein's work are correct, of course, but the difference in Epstein's and our work is that we have particularly stressed the percentage of free cholesterol instead of the ester cholesterol, since it has been shown that the percentage of free cholesterol is a physiologic constant in the normal individual. On the other hand, work in our laboratory has shown that along with the cholesterol esters there may be included a substance which is not entirely cholesterol ester and we believe that changes in the percentage of free cholesterol is a much better criterion. We are not as yet ready to report upon this undetermined substance

GANGRENE OF THE EXTREMITY IN THE DIABETIC*

ARTHUR A ZIEROLD, M D

MINNEAPOLIS, MINN

GANGRENE of the extremity in the diabetic manifests itself in two forms. The uncomplicated ischemic necrosis typical of the nondiabetic arteriosclerotic, commonly termed "dry gangrene" and the septic necrosis known as "moist gangrene."

The latter condition, which is the subject of this discussion, is not the result of a sudden vascular occlusion but is the culmination of a series of changes. Slowly, progressive intimal thickening permits the development of collateral circulation until eventually a delicate balance between life and death of the tissue is reached. When gangrene occurs it is more often the result of increased demands of the tissue cells due to the metabolic disturbances of sepsis and diabetes than to an immediate decrease in blood supply. Local bacterial invasion initiates or attends the development of this process, and soon becomes the dominating factor. The combination of sepsis and persistent but inadequate blood supply results in a moist spreading gangrene which untreated or unchecked causes death. If by way of treatment, early amputation is undertaken, it must be at a level which precludes further spread of the process or reoperation. This entails high amputation with its risk to life and the loss of excessive amounts of good tissue. If amputation is undertaken late in the progress of spreading gangrene, the mortality rate is high due to the combined effect of sepsis and diabetes. If, however, it be kept in mind that gangrene occurs not because of suddenly diminished blood supply to the part but because of suddenly increased cell needs and that if the tissue metabolism be returned to normal or nearly normal the blood supply would again be adequate, the necessity for amputation as the primary therapeutic procedure becomes less apparent. On the basis of this concept, it would appear reasonable that, in the presence of a spreading gangrene, if infection be eliminated, the diabetes could be controlled, and that if the diabetes with its disturbed metabolic processes and abnormal cell needs be controlled, gangrene would not recur.

Upon this assumption has been developed the following method of treatment which has obtained at the Minneapolis General Hospital during the past five years.

Upon admission to the surgical service with a spreading gangrene, the status of the patient's diabetes is determined, together with the incidental observations of ketosis, nitrogen balance, blood concentration and signs of dehydration. Normal hemoglobin and plasma protein levels are then restored by multiple transfusions and normal fluid balance is established—preferably by mouth or bowel. No great effort is made to control blood sugar levels

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

at this time, as in the presence of infection control of blood sugar levels and the products of abnormal metabolism is difficult and at times impossible. At the end of a 24-hour period, attention is directed to the local sepsis and gangrene. Under pentothal anesthesia, all infected or devitalized tissue is removed, together with any exposed bone. Contrary to the usual débridement, no attempt is made to save important structures, the goal being a base of live tissue with no gross evidence of infection and no pockets or overhanging skin borders. The wound is then covered with cod liver oil dressing and 12 to 24 hours later the patient is placed in a chair with the affected leg dependent and immersed to midcalf in 3 per cent saline at 100° F. The bath is alternated with bed rest at hourly intervals during the day. With the control of sepsis and diabetes, the gangrene is arrested and several days may be devoted to improving the patient's general condition. When the patient's temperature has remained at a normal level for three days, amputation may be undertaken as an elective procedure.

During the past five years, the mortality due to gangrene in the diabetic at the Minneapolis General Hospital has sharply decreased and we have come to accept the following doctrine:

(1) In the presence of sepsis and spreading gangrene, amputation should not be considered as a primary therapeutic measure.

(2) Amputation should be undertaken only as an elective operation, never as an emergency.

Of 92 cases treated during 1937 and 1938, 68 were treated by preliminary débridement and later by major amputation. Of these, eight or 11.7 per cent, died from pneumonia or coronary disease. None developed local infection and none necessitated reoperation following amputation. Twenty-four cases were treated by preliminary local excision with one death from bacteremia. Twelve refused later amputation and were discharged against advice. Others were discharged for a trial period. Of the entire group, the mortality was 9.7 per cent. Of the major amputations, 11.7 per cent, and of the preliminary excisions, 4.1 per cent.

At the University of Minnesota, where this procedure has been adopted during the past year, the amputation mortality has been decreased from 50 to 10 per cent.

DISCUSSION —DR WILLIAM E. GALLIE (Toronto, Canada) I wish to congratulate Doctor Zierold on his important and excellent presentation and to emphasize some of the points that he has made.

Soon after the discovery of insulin we adopted the policy of placing all the surgical diabetics under the care of one man, in order that we might determine as quickly as possible whether the new medical treatment would influence the surgical complications. As a result, Dr W. G. Murray has rapidly acquired a wide experience in the disease and has made important observations which agree in principle with those enumerated to-day by Doctor Zierold.

The outstanding result of the ten-years study has been that with adequate medical care one may confidently expect a great reduction of the mortality rate in so-called diabetic gangrene and also a great saving of limbs. Whereas,

formerly high amputation was performed at once in most cases of serious infection in the feet, the practice now is to control the diabetes with insulin and glucose and to treat the infection by wide incision and adequate drainage. The result is that in many cases the infection is controlled and the wounds ultimately heal.

In the more serious cases of spreading, moist gangrene our practice differs from Doctor Zierold's in that instead of a local operation on the infected gangrenous area we perform an immediate guillotine amputation about the middle of the calf, leaving the wound wide open for drainage. In a whole series of cases, this has resulted in immediate control of the infection and has allowed a subsequent formal amputation at a higher level without the risk that would attend such an operation at the height of the infective process. This, however, does not differ in principle from the method described by Doctor Zierold and I mention it only to emphasize what he has said.

DR LELAND S. MCKITTRICK (Boston) When I read Doctor Zierold's abstract in our printed program, I was quite distressed because I could not but feel that Doctor Zierold and I had very little in common in the management of this group of cases. After talking with him yesterday and after hearing his paper to-day, however, I would like to add my commendation to that of Doctor Gallie on what he has accomplished.

TABLE I

DEATH AFTER OPERATION UPON LOWER EXTREMITIES—806 PATIENTS

Cause	No. Cases	Per Cent	
		of Deaths	of All Patients
Infection	42	50	5.2
Cardiorenal (including pulmonary embolus)	37	44	4.6
Miscellaneous	5	6	0.6
Total	84	100	10.4

DEATH IN NONOPERATIVE TREATMENT OF LOWER EXTREMITIES

No. Patients	273	Deaths	12	Mortality	4.4 per cent
--------------	-----	--------	----	-----------	--------------

I think we all feel, as Doctor Gallie does, that it is of fundamental importance to distinguish between the group of cases whose arterial circulation is adequate and that more serious group where it is not. In this discussion I am limiting myself to the group of patients with inadequate circulation, and I think it is this group of patients that Doctor Zierold has been talking about.

Doctor Zierold has faced a serious problem that is not as uncommon as we might think. There is in the recent literature a summary of hospital mortality in which 12 hospital services in this country are listed. Eighteen to 75 per cent of these patients have died following amputations for gangrene. In eight of those 12 hospitals the mortality was over 50 per cent and in only one of them was it under 30 per cent.

As with Doctor Gallie, we have met this problem in a somewhat different way than Doctor Zierold, possibly because many of us in Boston who have been interested in this group of cases have not had to face a 60 per cent mortality. One of our former presidents, Dr. D. F. Jones, succeeded in bringing that 60 per cent mortality down to about 20 per cent before we were anything more than embryonic surgeons.

I should like to show a few statistics from which I will try to demonstrate certain facts which have influenced us in the management of these cases

In Table I are grouped the causes of death in all of the patients whose lower extremities we have operated upon. The mortality in this group is 10.4 per cent. About one-half of these died from infection. Four point six per cent, or roughly 5 per cent, of the patients operated upon have died from some form of cardiovascular disease. Interestingly enough, about one-half of our patients are not operated upon, and the mortality in this group is also about 5 per cent. This 5 per cent, then, is the irreducible minimum that Doctor Zierold has mentioned. We believe, however, that the mortality rate in excess of this figure for the most part due to late, inadequate, or improper treatment.

TABLE II

FIRST 100 AMPUTATIONS FOR DIABETIC GANGRENE	
Dead	92
Living	8
Living 3 years	58%
Living 5 years	35%
Average duration of life (92 patients) 42.7 months	

Table II presents another phase of the problem. Of the first 100 patients who left the hospital following amputation for gangrene, eight are still alive. However, one-half of the patients were already dead at the end of three years and at the end of five years only one out of three patients was alive. The average length of life after operation in the 92 dead patients was three and one-half years. In other words, the diabetic patient with gangrene looks forward after amputation to an average life expectancy of only three and one-half years. We must, therefore, be careful in whatever we plan not to have them spend too much of this time within the hospital walls.

TABLE III

TYPE OF AMPUTATION IN 503 PATIENTS WITH DIABETIC GANGRENE

Level	Cases	Per Cent of Total	Deaths	Mortality Per Cent
Toe	53	10.5	4	7.5
Toe then major oper	35	7.0	4	11.4
Lower leg	36	7.2	1	2.8
Guillotine	33	6.6	14	42.4
Gritti-Stokes	80	15.9	11	13.8
Thigh	266	52.9	31	11.7
Totals	503		65	12.9

Table III shows the type of operations performed upon 503 diabetic patients with gangrene from 1923 to 1938. I should like to call your attention to the 33 patients (7 per cent of the group) who have had a guillotine amputation. In other words, in the group of patients that we see who are in need of an amputation but whose general condition is so poor or whose local infection is so extensive as to contraindicate primary closure, we would not undertake the local procedure that Doctor Zierold advises, but instead a guillotine amputation through the upper third of the lower leg, planning to follow this by a higher amputation at a later date.

There is one other point that I should like to make. Interestingly enough,

there is no agreement among surgeons, at the present time, as to what represents the safest, surest, and simplest closed amputation for a diabetic patient who is such a poor risk that one can be confident that he will never use an artificial limb. You will notice in Table III that approximately half of our patients have a primary, closed supracondylar amputation, with a mortality of 11.7 per cent. This operation has been elected because it represents the amputation which, in our hands, is followed by the highest incidence of healing *per primam* and the shortest period of hospitalization.

DR FRANK L. MELENEY (New York, N. Y.) In this condition, we are dealing with a problem of infection, and that concerns bacteria. I have been surprised that Doctor Zierold did not make any mention of the bacteriology of these infections, because I think that that is one of the fundamental bases upon which the form of treatment in any given case must be determined. Here we have a condition in which there are a number of important organisms which are responsible for death, and it is essential, it seems to me, for the surgeon to know with what organisms he has to deal before instituting treatment.

Anaerobic bacteriology is particularly applicable here, because the Welch bacillus and the anaerobic streptococci are particularly common. Also, in this condition, we have the factor of bacterial symbiosis or synergism. In diabetic gangrene, there is almost always a mixture of organisms, and I believe that those organisms working together make the infection infinitely more virulent than it would be if any of the organisms were to be found in pure culture. In some cases in which gas gangrene or some other overwhelming infection is present when the patient is admitted, a quick guillotine operation is indicated without waiting for bacterial cultures. However, in most cases time is afforded to make a complete analysis of the bacterial flora.

We are making it a routine procedure to establish, as soon as possible, the number and kind of organisms that are present in all cases of diabetic gangrene. During that time, the preliminary preparation of the patient, from the point of view of the diabetes, can be carried out. Cultures should be taken not from one place but from many places in the gangrenous area. Thus, all of the organisms with which one has to deal can be determined. Of course, all of the organisms which can be found on the surface are not necessarily important. Many of these may not have invaded the tissues deeply, but certainly there is no organism which is deep which cannot be found on the surface. If the hemolytic streptococcus or the Welch bacillus or any of the anaerobic streptococci are known to be present, then the possibility of their later developing an infection at the site of amputation should be in the mind of the surgeon. He will anticipate it, be ready for it, and, if possible, prevent it. To be forewarned is to be forearmed. No one should be surprised if gas gangrene develops in an amputation stump.

Also, if cultures are taken at the time of, and at the site of amputation, the surgeon may know what organisms to expect if an infection develops there secondarily. It seems to me to be reasonable to plan on an open amputation if the Welch bacillus, if the hemolytic streptococcus, or if any of the micro-aerophilic or anaerobic streptococci are found in the original gangrene. Secondary closure can then be performed at the site of amputation, if cultures taken at the time of amputation show no evidence of the presence of those organisms after 24, 48, or 72 hours, and the wound can be prepared to be closed in that time with the expectation of primary healing. If those organisms are not present in the original gangrene, the surgeon can close his amputation with much more feeling of satisfaction and equanimity and with

every expectation that his wound will heal without subsequent infection. The level of amputation should depend largely upon the level of adequate circulation.

The *Staphylococcus aureus* is another organism which may invade, and if present, the surgeon should know that there is a possibility of its invasion. If he closes the wound at the primary amputation, then he must be particularly careful to observe the earliest signs of inflammation. If infection develops in the wound which he has closed, then he should open it and treat it specifically if he knows the organism which is likely to be present.

Zinc peroxide is often of service in these cases. It may be employed to hold the local lesion *in statu quo* while the general diabetic condition of the patient is being brought under control. Later, if the Welch bacillus or the anaerobic streptococcus or the hemolytic streptococcus is found to be present at the site of amputation, zinc peroxide should be used for immediate and specific treatment.

In short, we have here a complicated problem with three major factors: diabetes, blocked arteries and infection. All of these factors must be given serious consideration if we are going to reduce the mortality in these cases to a reasonable figure.

DR HERMAN E. PEARSE (Rochester, N. Y.) As with Doctor McKittrick and Doctor Gallie, we have approached the problem in a little different manner. If there is any difference, it would appear to be more apparent than real due to confusion in terminology. For this reason I would like to make a plea to abandon the term "diabetic gangrene." It covers a multitude of conditions which are not treated alike. In fact, the management of these cases is predicated not on the diabetes nor on the gangrene, but on the state of the circulation.

You all know that under the term "diabetic gangrene" are included such diverse conditions as dry, senile gangrene, and the gangrene from thrombosis or infection in the presence of an extremely good circulation. In the first instance, local surgery is apt to be dangerous. In the latter instance, local surgery is obligatory, because with a good circulation, local operation will frequently cure the individual and avoid an amputation. In between these two extremes there are all varieties of combination of infection and circulatory deficit. Unfortunately, one cannot say quantitatively how much the circulation is impaired. It would clarify this situation greatly if we might determine that an individual has a 30 per cent deficit or an 80 per cent deficit in his circulation, then we would use a uniform nomenclature.

It would appear desirable, then, not to include all cases under the one term of "diabetic gangrene." If this is done, we can segregate the patients that would profit by local measures. I am sure the greatest hope for the individual who has gangrene with a competent circulation is in the local surgery which avoids loss of the limb.

DR ALTON OCHSNER (New Orleans, La.) We have been able to decrease the mortality rate in these cases in our institution by having them under the care of one man, Doctor Charbonnet, who, because of his preliminary training in internal medicine, is particularly able to handle them effectively. We have divided the cases of diabetic gangrene into three groups. One, in which there is a progressive gangrene associated with infection, another, in which there is considerable vascular competence, and the third, in which there is no vascular competence and in which the infection is mild. In the first group, we are convinced that early amputation is life-saving as

DIABETIC GANGRENE

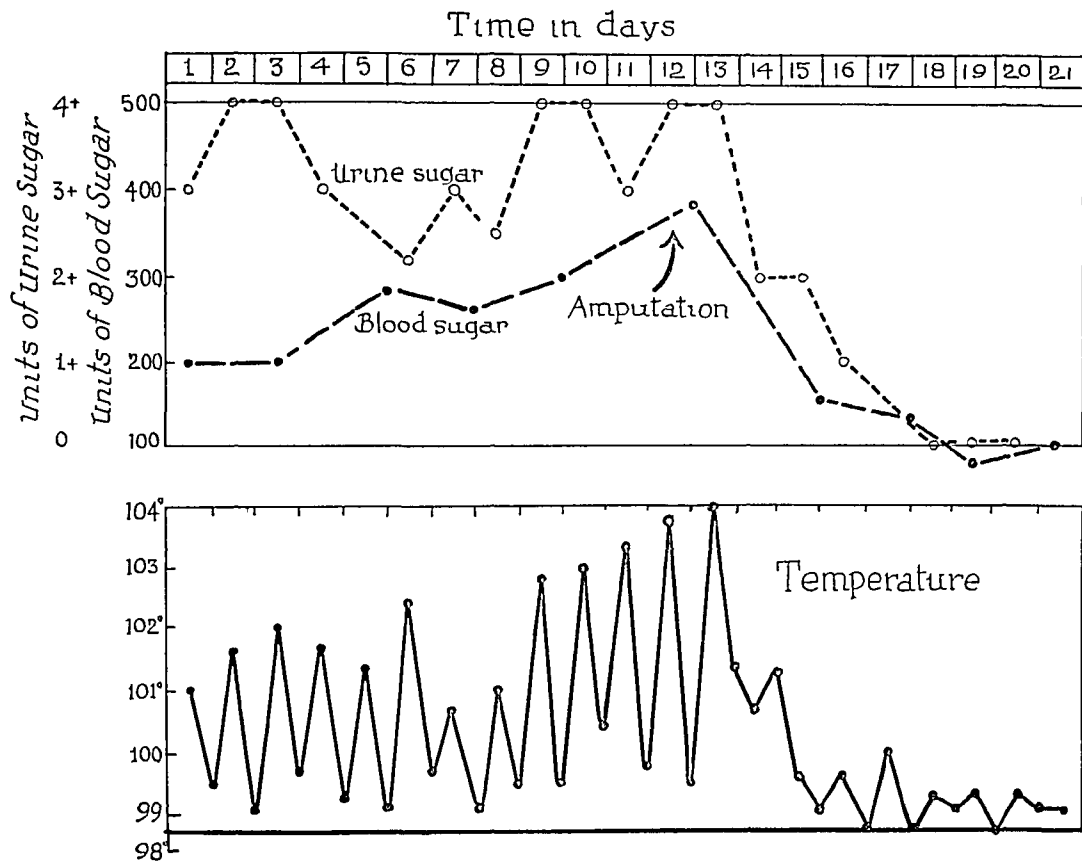


CHART 1—Clinical course of a case of diabetic gangrene in which conservative therapy was employed, showing persistence of hyperglycemia, glycosuria and fever in spite of attempts to control the diabetes. Shortly after removal of the infected gangrenous foot, temperature, blood sugar, and urinary findings became normal.

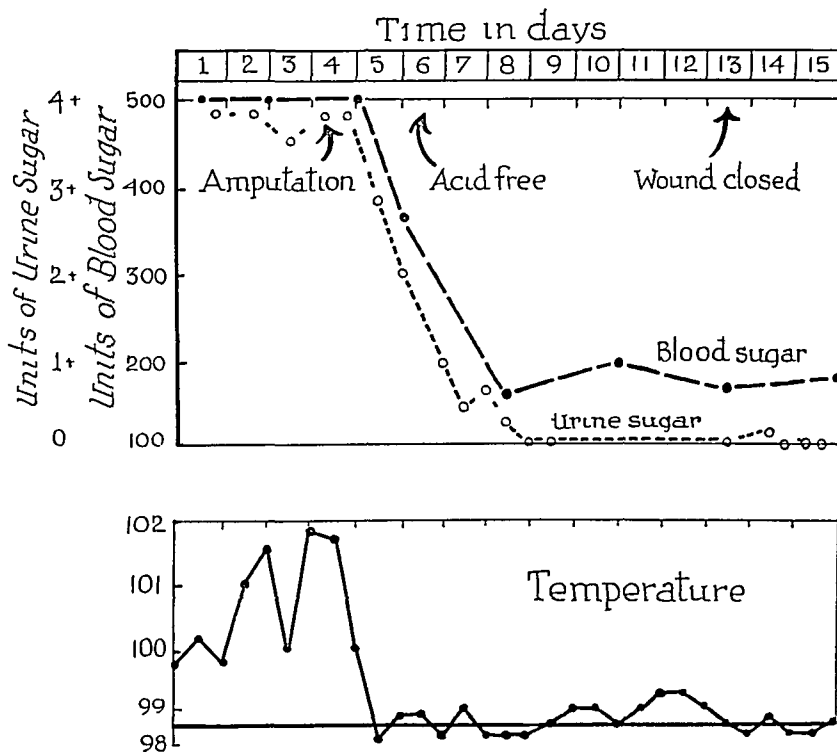


CHART 2—Clinical course of severe diabetic gangrene, illustrating the prompt return to normal of temperature, blood sugar and urinary findings immediately after amputation. The diabetes in this case was much more severe than that illustrated in Chart 1, although the decrease in symptoms was very prompt following removal of the infected foot.

illustrated by the two cases whose clinical course is presented in Charts 1 and 2

I would like to discuss the second group of cases to which Doctor Pearse has already referred

Contrary to what is commonly thought, the patient whose peripheral pulsations are absent need not necessarily have an incompetent vascularity. I think we as surgeons pay too little attention to the possibility of a vasospastic influence originating in an infected focus in an extremity. Because of this, in these patients in whom there is not the urgency for amputation we have done a novocain block of their lumbar sympathetic ganglia and studied by means of plethysmographic determinations the pulsations of the arterioles of the toe, and in this way determined the degree of vascular competence.

In those cases in which there was a considerable vascular competence, in spite of the fact that there may be obliteration of the larger vessels, as evidenced by absence of pulsation, we have felt ultraconservatism was justified. Following the determination of vascular competence by means of novocain block the sympathetic ganglia are blocked with alcohol which produces vasodilatation for six to eight months.

I feel if one will consider the possibility of vasospasm in these patients in whom there is a necrosis or infection and offset the vasospasm by first novocain block and later alcohol block of the sympathetic ganglia, the possibility of saving these extremities and getting a good extremity can be greatly enhanced.

DR ARTHUR A ZIEROLD (closing) It is interesting in traveling to look around and see how many have arrived at the same destination but by different routes. I feel a certain sense of gratification in that Doctors Gallie, McKittrick, and Ochsner have arrived at approximately the same destination, although by different routes.

There is little that I can add to the discussion other than to recall one statement, and that is that we are not concerned solely with an alteration in blood supply, but we are concerned in an alteration in the cell needs and the cell metabolism.

As to the efficacy of the different procedures, I perhaps neglected to intimate that this was in my mind, namely, a method of treatment of gangrene in the diabetic, and not *the* method. I appreciate very much the manner in which you have received this communication.

FIBROMA OF THE OVARY WITH ASCITES AND HYDROTHORAX^{*}

A FURTHER REPORT

JOE VINCENT MEIGS, M D

BOSTON, MASS

SINCE the first report of this syndrome by Meigs and Cass,¹⁰ in 1937, two articles have added three recent cases. One case has recently been reported in full by Rhoads and Terrell,¹² and two others are recorded by Weld.¹⁸ A further search in the literature, stimulated by a paper of Dr. Muiel B. McIlrath,⁸ in 1937, has brought to light two much older cases. A case reported by Dr. U. J. Salmon,¹⁴ in 1934, is of the same nature. Recently, Dr. Richard H. Miller¹¹ and Dr. Donald Macomber⁷ have each operated upon a patient with this entity. These additions to the report of Meigs and Cass bring the recorded cases to 15. Thus it is clearly established that this condition is a definite entity and deserves to be called a syndrome. The reason for the fluid in the chest as well as the abdomen is no clearer and even the availability of an autopsied case fails to throw light on the problem.

The importance of this syndrome is great, for unexplained pleurisy and ascites may be caused by a tumor that can be overlooked even on careful examination. Abdominal paracentesis may be necessary before the ovarian tumor can be felt. The case of Rhoads and Terrell (No. 15) demonstrates how easily a patient could be allowed to die with a diagnosis of inoperable malignancy. It is certain that if 15 cases have been found there must be many others, especially as six of the 15 have been operated upon by members of the Massachusetts General Hospital Staff. It is certain, therefore, that throughout the world many patients with this curable lesion have been doomed to a slow death.

In patients with abdominal tumors and fluid in the chest it is very important that the chest be tapped and roentgenograms then taken. These may show, as they did in Case 10, that when the fluid was removed no evidence of metastatic malignancy was found. If such roentgenologic study, plus examination of the patient after abdominal paracentesis, could be made a routine, then other unrecognized cases would be separated from the group of metastatic malignancies.

In no text-book on gynecology or pathology has there been definite mention of fluid in the chest being found in conjunction with fibroma of the ovary. Fluid in the abdomen is mentioned many times, but not fluid in the chest. In articles by Hoon,⁴ McIlrath,⁸ Rhoads and Terrell,¹² Weld,¹⁸ and in my⁹ own book on pelvic tumors, the presence of chest fluid is described. Cullingworth's¹ case, reported in 1879, is the first description of this interesting entity. His patient died, and the autopsy does not explain how the fluid traveled from the abdomen to the chest, a question that is important to solve.

^{*} Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

Symptomatology—The most frequent symptoms of this lesion are difficulty in breathing and a sense of pressure and weight in the abdomen. Most patients had dyspnea, some over long periods of time (months). The presence of ascites, or at least of an abdominal mass, was known to have existed in one case (Case 15) for eight years and in another (Case 1) for five years. Table I shows that abdominal symptoms may be of long or short duration. A number of patients complained of abnormal bleeding—an evidence of failing ovarian function. Small ovarian cysts in normal or tumorous ovaries may be considered such evidence. These cysts, follicle in type microscopically, resemble those seen in other solid tumors of the ovary such as Krukenberg tumors, and in the latter cases abnormal bleeding may be present. As in metropathia hemorrhagica, failing ovarian function is manifest by a persistent follicle cyst. Symptoms of dyspnea, pain and discomfort in the chest, and the presence of abdominal distention should draw attention to this lesion.

TABLE I

DURATION OF KNOWLEDGE OF ABDOMINAL MASS OR DURATION OF ABDOMINAL SYMPTOMS

Case 1	5 years	Case 8	1 year
Case 2	3 years	Case 9	3 months
Case 3	2 weeks	Case 10	3 months
Case 4	1 year	Case 11	Several years
Case 5	1 year	Case 12	2 months
Case 6	3 years	Case 13	6 weeks
Case 7	At admission	Case 14	2 years
Case 15		8 years	

Physical Examination—Physical or roentgenologic examination disclosed the presence of fluid in the chest in every case. In some it was only demonstrated roentgenologically, but in 12 cases it was demonstrated by tapping the chest and obtaining fluid. In only six was the abdomen tapped to prove the presence of fluid, but at operation, abdominal fluid was found in all cases. In all patients, but in some only following abdominal paracentesis, a mass was found in the abdomen. Cachexia is not uncommon and is due to rapid dehydration because of the quick reaccumulation of fluid in the chest and abdomen after tapping.

Laboratory Data—The laboratory findings in subsequent cases add nothing to those reported by Meigs and Cass in 1937. The specific gravity of the fluid is that of a transudate, the presence of lymphocytes is noted, and the absence of tumor cells whenever looked for. Numerous attempts to obtain positive guinea-pig tests failed and in no instance was tuberculosis proved. Apparently the fluid is not in the nature of an inflammatory reaction. The blood studies were of no significance, and the elevation of the temperature was minimum. The serum protein in Case 10 was 7.1 mg and in Case 15 it was 6.9 before operation and 7.3 at time of discharge. These figures are within normal limits.

Preoperative Treatment—In many cases the chest and abdomen were tapped numerous times. Table II shows that abdominal paracenteses were performed about half as often as chest taps. It is to be noted that the chest

T A B L E 11

SYNOPSIS OF 15 CASES WITH FIBROMA OF THE OVARY WHICH EVIDENCED SIGNS OR SYMPTOMS OF FLUID IN THE ABDOMEN AND CHEST

Case No and Date	Author	Age	Status	Children	Chief Complaint	Tumor	Location of Effusion in Thorax	Thora-centesis	Ab-dominal Para-centesis	Fluid at Operation
No 1, March, 1879	Cullingworth ¹	36	M	Yes	Metrothragia Dyspnea Col-lapse	Bilateral	Left	0	0	Died without operation
No 2, April, 1901	M G H ¹⁰	42	S	None	Pain in right chest	Ovary	Right	4	1	Considerable Autopsy straw-colored ascitic fluid
No 3, June, 1902	M G H ¹⁰	55	M	Yes	Pleurisy	Right	Right	5	0	6 to 8 quarts as-citic fluid
No 4, Oct., 1908	M G H ¹⁰	38	M	Yes	Pain in shoulder, especially on left	Left	Right and left	7	4	Several quarts ascitic fluid
No 5, July, 1917	Mayo ⁴	36	M	Yes	Bloating of ab-domen Cough Loss of strength	Ovary	Left	1	0	Marked ascites
No 6, Nov., 1920	Mayo ⁴	53	M	None	Bloating Pain between scapulae	Right	Right	3	1	Several liters ascitic fluid
No 7, March, 1926	Leo ⁵	64	?	?	Dyspnea Pain in chest	Left	Right	Repeated	0	Large amount of ascitic fluid
No 8, April, 1928	de Rouville, ¹³ <i>et al</i>	58	M	Yes	Cough Emacia-tion	Right	Left	1	9	1,000 cc ascitic fluid
No 9, April, 1932	Salmon ¹⁴	52	M	?	Abdominal mass, and cramps	Right	Right	3	0	500 cc ascitic fluid
No 10, Aug., 1934	M G H ¹⁰	52	S	None	Dyspnea Change in bowel habits	Left	Right	Repeated	1	Large amount yellow ascitic fluid
No 11, July, 1936	Miller ¹¹	60	S	None	Pressure Weak-ness Dis-ability	Right	?	3	0	
No 12, Aug., 1936	Weld ¹⁸	55	?	?	Swelling of abdomen	Bilateral	Right	0	0	3,500 cc ascitic fluid
No 13, Sept., 1936	Weld ¹⁸	50	M	?	Enlargement of abdomen	Right	Right	0	0	Blood-tinged ascitic fluid
No 14, Jan., 1937	Macomber ⁷	33	S	None	Tumor in ab-domen	Left	Right	1	1	Two quarts ascitic fluid
No 15, Feb., 1937	Rhoads and Terrell ¹²	57	M	Yes	Dyspnea Shortness of breath Fatigue	Right	Right	5	0	750 cc ascitic fluid

fluid reaccumulated with great rapidity, and relief was short in most instances

Operative Pathology—In all but two instances, a single fibroma of the ovary was found at operation. Since the first report, two patients have been found with bilateral fibromata. One would immediately suspect that these bilateral fibromata might be Krukenberg tumors of the ovary, i.e., metastases in the ovary from a carcinoma of the stomach, except for the fact that one patient with bilateral tumors (Case 1) died, and at autopsy no mention was made of a gastric neoplasm. Krukenberg's original name for his tumor is "fibrosarcoma ovarii mucocellulare carcinomatodes", therefore, it is reasonable to assume that they might easily be confused with true fibromata of the ovary. The other patient (Case 12) is known to have been well at least three months after her operation, and there has been no suspicion of gastric cancer. Abdominal fluid was found in every case, varying from small to very large amounts, and its color ranging from the usual straw color to serosanguinous. The tumors varied in size from 9 to well over 20 cm., and many of them were reported as being wedged in the pelvis.

There were no fatalities following the operation, and convalescence in nearly all instances was uncomplicated. In three patients fluid remained after operation but gradually receded and vanished. In only one patient (Case 6) was it necessary to do a chest tap after operation and this was done directly afterward. The patient who came to autopsy died suddenly while in the hospital and before any surgery was undertaken. She was in the hospital under observation for six months and finally died of severe dyspnea and a generalized collapse. It is most probable that with our present knowledge, this patient would have survived.

Histologic Pathology—All tumors were fibromata and were made up of interlacing bands of tough, white connective tissue with cystic areas. The cysts represent either areas of liquefaction following interference with the blood supply or follicle cysts that have grown large and have not been obliterated.

The fibrous connective tissue of the ovarian stroma, derived as it is from the primitive mesenchyme of the embryonic gonad, gives rise to the fibroma of the ovary. The fibromata under discussion are all simple tumors and no evidence of luteinization as in "xanthofibroma cellulare" has been demonstrated. It is probable that the abnormal bleeding occasionally occurring in this syndrome is due to changes of a proliferative type in the endometrium (Case 11) due to persistent follicle cysts rather than to lutein changes in the fibroma.

End-Results—Except for one patient that died without being operated upon, the end-results are uniformly excellent, and in no instance has it been necessary for the patient to return for removal of fluid from the chest or abdomen. Now that 14 cases have been seen and followed after operation it is obvious that the treatment is satisfactory. If this entity is suspected in a patient, an effort should be made to prove it, and no patient should be refused exploratory operation in order to confirm the suspected diagnosis.

FIBROMA OF OVARY

A CHRONOLOGIC PRESENTATION OF ALL KNOWN CASE REPORTS (15) OF PATIENTS WITH FIBROMA OF THE OVARY COMPLICATED BY ASCITES AND HYDROTHORAX

Case 1—Cullingworth¹ A K, age 35, a widow, was admitted to St Mary's Hospital, Manchester, England, March 11, 1879. She stated that she had had a swelling in the right groin, which she first noticed after the birth of her fifth child five years before. This, however, had disappeared until December, 1878, when she again noticed it. At the time of admission, she was having a slight uterine hemorrhage, which had been present continuously for about three months, previous to which time she had menstruated regularly. The patient had a florid, healthy complexion, and had not suffered in her general health.

Physical Examination—Two hard, solid, nodulated tumors were discovered in the pelvis. One occupied the right side and extended a little over to the left, lying in front of the uterus and immediately beneath the abdominal wall. It was freely movable within a limited area. The second tumor, larger than the first, lay behind the uterus, with its smaller end dipping down into Douglas's pouch which it completely filled, and its larger end rising up above the level of the fundus uteri. The tumors were not adherent to the surrounding parts, and there was no fluid noted, at this time, in the peritoneal cavity.

The uterine hemorrhage finally ceased about the middle of June, 1879, from which time the patient's health rapidly declined. She lost weight, and ascites supervened to such an extent that on being admitted as an inpatient, at the end of July, the girth of the abdomen at the umbilicus was 39½ inches (100.3 cm). By August 12, 1879, it had increased to 42½ inches (108 cm). She suffered also from pleurisy, first on the left side, where effusion took place, and subsequently over the greater part of the lower lobe of the right side, where loud friction sounds were audible to within a short time of her death. On September 10, 1879, the patient became suddenly worse, with symptoms of intense dyspnea and general collapse. She died on the following day.

Autopsy—The left pleural cavity was found full of fluid, and the whole of the left lung entirely collapsed. On the right side, the lower lobe was firmly attached by recently formed adhesions to the diaphragm and chest wall, and the whole lung was congested and edematous.

There was a large quantity of fluid in the peritoneal cavity, and the peritoneum was thickened and opaque. The abdominal and pelvic viscera were healthy with the exception of the ovaries, each of which had become transformed into a solid tumor. The tumor of the right ovary lay in front of the uterus and right broad ligament, crossing over to the left of the median line. That of the left ovary was wedged firmly in the pelvis behind the uterus, some force being required to extract it. Neither tumor was adherent. Both were solid throughout, with the exception of a serous cyst, about one inch in diameter, which had formed in the substance of the growth on the right side, close beneath the capsule. The weights and measurement of the tumors were as follows:

	Weight	Length	Breadth	Thickness
Right	9 oz (255 Gm)	5 ins (12.7 cm)	3¾ ins (9.5 cm)	2¼ ins (5.7 cm)
Left	22 oz (624 Gm)	6 ins (15.2 cm)	5 ins (12.7 cm)	3 ins (7.6 cm)

The tumors were firm and nodulated, whitish-gray in color, with a smooth, glistening surface. It was evident that they had replaced the ovaries, no portion of the normal tissue of the ovary remaining. The cut surface was firm, dry, and homogeneous, of a whitish-yellow appearance, and presented numerous small openings, of the size of a pin's head, which were evidently small cysts, while the larger cyst, already described as existing at one part of the periphery, was seen to be filled with a glairy fluid. Numerous whitish bands, irregular in their course, passed in from the fibrous capsule and subdivided the tumor into lobes, which in many places had a concentric arrangement. The

portions of the tumor enclosed within these trabeculae were equally firm, presented a finely fibrous appearance, and were of a somewhat yellowish tinge

The tumors were examined microscopically in the pathologic laboratory of Owens College, by Doctor Dreschfeld, who has kindly furnished the following report "The microscopic structure is best seen in sections cut from a part of the tumor which had been placed at once in Muller's fluid and hardened. This section shows the tumor to consist of fine and coarse fibers, along with cellular elements, blood vessels, and small microscopic cysts. The blood vessels are numerous, the larger ones consist of fully-formed arteries and veins, with well-developed muscular walls, the smaller ones are found to be capillaries. The section also shows the existence of larger spaces, bounded by fine fibers which form a kind of lining membrane, they are not lined by endothelium, nor do they contain other than fluid contents, their well-formed fibrous boundary, however, shows them to be cysts and not mere breaks in the tissue. In a section prepared from a portion of the tumor hardened in spirits, the arrangement of the fibrous tissue is seen to better advantage, but the cellular elements and blood vessels appear much shrunken. The tumor is a fibroma. The cysts not being bounded by distinct epithelium are probably due to cystic degeneration of the primary tumor masses."

Case 2—Massachusetts General Hospital. A female, age 42, single, entered the hospital, April 29, 1901, complaining of pain in the right chest of one week's duration. Pain had increased gradually and she had become short of breath. The catamenial history was negative until three years before, when she occasionally skipped a month. She had had no cough, dyspnea, or pain before the present illness.

Physical Examination showed a well-developed and well-nourished woman. The heart was negative. There was flatness over the right chest throughout, with diminished voice sound and fremitus. Respiration was also much diminished. The left chest was negative. The abdomen showed a large, hard mass extending up to the umbilicus. Several nodules, like small fibroids, could be felt over it.

On April 30, 1901, 80 ounces of clear fluid were aspirated from the right chest. This made the patient much more comfortable, but physical signs showed that there was still considerable fluid present. On May 3, 1901, 62 ounces were withdrawn, with much relief to the patient. (An inoculation from this chest fluid was made into a guinea-pig. The animal was found dead on May 21, 1901, and an autopsy was performed which showed no evidence of tuberculosis.) The patient made an uninterrupted convalescence and was discharged, much relieved, May 7, 1901.

On May 28, 1901, the patient was readmitted, complaining of cough with considerable yellowish sputum, without blood. For the past two weeks dyspnea had again steadily progressed, so that she was unable to lie on the left side, and could walk only with difficulty.

Physical Examination showed both lungs symmetrical with expansion of the left greater than the right. There was right chest flatness below the level of the spine of the scapular and second rib in front with dulness above these limits and tactile fremitus diminished above and absent below. The interspaces were slightly fuller over the right chest. Respiration was feeble and with diminished voice sounds. No râles were heard. Heart impulse was palpable in the fifth space in the anterior axillary line and dulness corresponded 15 cm from the midsternum. The sounds were of good quality and there were no murmurs. Pulses were equal and synchronous, of low tension, small volume, and regular. The abdomen was convex both ways, abruptly prominent, and slightly fuller in the right lower quadrant. A hard mass could be felt rising from the pelvis to two fingers' breadth from the anterior superior spine on the right, thence to two fingers' breadth above the navel line and descending to the left, this mass was hard, nontender, nonfluctuant, and movable laterally and anteroposteriorly. The flanks were tympanitic. Vaginal examination showed that the introitus admitted two fingers with difficulty. The cervix was low, of normal size, conical, and pointed perpendicular to axis of the vagina. The same hard mass was felt in the left vault and the posterior

culdesac The body of the uterus could not be made out Hemoglobin was 85 per cent and the white blood count 11,000 The urine was normal

On May 29, the patient was uncomfortable from dyspnea all night The right chest was tapped and 68½ ounces of clear, straw-colored fluid withdrawn, with a specific gravity of 1.016, slightly alkaline, and the albumin content was 3.2 per cent A slight sediment contained mostly fibrin flakes with a few degenerated epithelial cells and leukocytes No organisms were found

On June 1, the right chest was again tapped and 58 ounces were withdrawn The fluid was clear and straw-colored, with a specific gravity of 1.017, slightly alkaline, albumin 3 per cent

On June 3, a surgical drainage of the thoracic effusion was done under cocaine anesthesia An incision two inches long was made through the skin A needle was introduced, followed by the escape of yellow fluid A knife was passed in and an incision was made through the intercostal muscles and pleura between the seventh and eighth ribs Two small tubes were introduced and about 48 ounces were evacuated

On June 10, the patient spent a rather uncomfortable day She was not draining so much, the abdominal growth seemed increasing in size, and there was a question of ascitic fluid She was losing ground a little On June 12, she had considerable pain and was draining profusely Her abdomen was tapped and the fluid injected into a guinea-pig and found to be nontubercular By July 2, the patient had lost strength Her feet were swollen The thoracic cavity was washed out every day and four ounces of foul pus withdrawn There was considerable distention of the abdomen The abdomen was tapped again on July 7, and over six pints of reddish fluid were withdrawn On August 13, 1901, the patient was discharged much relieved

On September 18, 1901, the patient reentered the hospital for operation for an abdominal tumor, considered to be a fibroid of the uterus She had continued to improve and had gained eight pounds in the two weeks previous to admission

Under ether anesthesia, an ovarian tumor was removed, September 20, 1901 A long, median suprapubic incision was made and the peritoneum opened with immediate escape of considerable straw-colored fluid A large whitish mass presented After some manipulation, with the breaking up of adhesions, a mass about the size of a child's head, very solid and whitish in color, was removed The pedicle, including the tube, was tied off with heavy silk On October 19, the patient was discharged well and in good condition

The pathologic report showed the mass to be an irregularly rounded tumor, measuring 20 cm in greatest diameter and weighing 2,440 Gm On section, the surface was moist, with numerous small cystic cavities, and on one side a remnant of ovarian tissue could be identified The outer surface was covered with thin, fibrous membrane in which were numerous thin-walled veins and some slight adhesions The consistency was firm, almost cartilaginous, and at one place the surface was deeply fissured The tube was normal Microscopic examination showed the structure to be made up of interlacing masses of fibrous and muscular tissue, in places quite cellular, in others less so

Throughout the growth were chunk-like spaces which were evidently of vascular origin A diagnosis of fibromyoma was made

In December, 1902, the patient wrote that she was in excellent health and had been married the previous September

Case 3—Massachusetts General Hospital A female, age 55, married, para 1, entered the hospital, June 9, 1902 Five months previously, she had had "pleurisy" with a slight cough and pain in the lower chest in front, not especially connected with respiration She was confined to bed for three months, and had never been strong since She was tapped five times in the right back and two to four quarts of fluid were removed For the past two weeks, her abdomen, which had always been prominent, had increased rapidly in size She was constipated but her bowels moved well with

cathartics. She had occasional vomiting without blood and considerable abdominal discomfort. Three years before, she had noticed a tumor moving from side to side in the lower abdomen, it moved spontaneously and felt "like a baby." She had no pain or discomfort from this mass.

Physical Examination showed a well-developed and poorly nourished woman, with fairly good color. She had a small, rapid pulse of low tension. The heart was negative. Respirations were slightly harsh all over, with an occasional rale, especially in the right base. There was dullness in the right axilla and right back below the angle of the scapula, with practically no respiration or voice sounds. Liver dullness began at the fifth rib in front. The abdomen was greatly distended, with shifting dullness in the flanks and tympany in the upper portion of the abdomen. There was a marked fluid wave. Nothing was palpable through the distended abdominal wall. There was slight dilatation of superficial veins. No edema of legs or face was noted. Pelvic examination showed a polyp, the size of an English walnut, presenting at the vulva with a narrow pedicle springing from the posterior wall of the interior of the cervix. Bimanual examination was unsatisfactory, the uterus appeared to be in good position and not enlarged. The culdesacs were full of fluid. There was slight tenderness in the left culdesac.

At operation, on June 10, under ether anesthesia, an incision was made in the median line below the umbilicus. The peritoneum was opened and six to eight quarts of yellow, clear fluid escaped. A mass in the right side was delivered into the wound and found to be an ovary the size of a coconut. A few adhesions were separated. The ovary and part of the tube were removed. Manual examination of other organs showed them to be apparently normal. On June 26, the patient was discharged well.

The pathologic report showed an irregular, lobulated mass covered for the most part by peritoneum. Weight 1 kg, 14 cm in diameter. Adherent to one side was the fallopian tube, 6 cm long, apparently normal. In one place the omentum, which contained many large vessels, was adherent. On section, there were masses of grayish tissue separated by bands of edematous connective tissue. A diagnosis of edematous fibromyoma was made. The patient died, October 25, 1913, 11 years postoperatively. The cause of death was given as senility and ventral hernia.

Case 4—Massachusetts General Hospital. Female, age 38, married, para 2, entered the hospital, October 9, 1908, complaining of not having felt well for the past year. She had had some pain in her shoulders and back. Seven months previously she consulted a physician because of pain in the left side, which she described as sharp and knife-like and which prevented sleep. A left pleural effusion was found, the chest was tapped, and two quarts of fluid were withdrawn. She had been at rest, had been out of doors, and had had an extra diet with improvement, but the fluid returned very rapidly. About four weeks prior to her admission, she had noticed the abdomen increasing in size, this continued up to the time of admission. She had had some dyspnea on exertion for a good many years, but it had been worse since the fluid in the chest appeared and had become very greatly increased since the fluid in the abdomen had been noticed. She could not lie down flat but could walk up the stairs. For two days previous to her admission, her feet and legs had been swollen. A note from her local physician stated that her urine was normal. Three examinations of the sputum had been negative for tubercle bacilli.

Twelve months previously, a physician had found a uterine fibroid, and for two to three years previously she had felt something wrong in the region of the uterus. She had had no treatment. There had been no ascites.

Physical Examination showed a well-developed and well-nourished woman, with skin and mucous membranes of good color. She breathed easily in semirecumbent position or bed rest. No cervical, axillary, or inguinal nodes were palpable. The heart apex impulse was not seen or felt, but pulsation was felt best to the right of the sternum. The left border of dullness was not determined. The right border, in

the fourth interspace, was 65 cm to the right of the midsternum. Sounds were best heard to the right of the sternum. They were regular and of good quality. There were no murmurs. Pulses were synchronous, equal, regular, and of fair volume and tension. The left chest was flat throughout and breathing was distant and at the base behind close to the spine there was egophony. Tactile fremitus was absent. There was flatness below the fifth rib in the mammary line on the right. The line of flatness extended around the chest in a horizontal line to 25 cm below the lower angle of the scapula in the back. Breathing throughout the right chest was normal. The abdomen was very prominent, the greatest girth being midway between the umbilicus and pubes, and measured 110 cm. The umbilicus was flush. The abdomen was tense but not rigid. No masses could be felt. No tenderness or shifting dullness was noted. A fluid wave was obtained. Liver dullness began at the fifth rib, the lower border not being determined. There was slight, soft edema of the feet and ankles.

On October 10, the patient's abdomen was tapped, 18 pints of clear yellow fluid being obtained, and the end of the trocar impinged against a solid tumor which somewhat interfered with the flow.

Report of the ascitic fluid showed nine quarts of clear straw-colored fluid, alkaline, specific gravity 1.018, albumin 2.4 per cent. A culture was taken. Smears showed a predominance of lymphocytes. Some of the fluid was injected into a guinea-pig, the animal was killed, November 14, 1908, and an autopsy showed no tuberculosis. On October 19, a skin tuberculin test was negative after 48 hours. The patient complained of abdominal pain radiating to the right chest, nausea, and frequent vomiting. She had no fever and there was no change in the physical signs.

The fluid in the abdomen increased while the fluid in the chest seemed to be less. On October 25, the patient's abdomen was again tapped, low down in the right flank, and 14 pints and nine ounces of a clear yellow fluid were obtained. Girth before tapping measured 100 cm and after tapping 83 cm. Report of the ascitic fluid showed slightly cloudy, straw-colored fluid without clot, alkaline, specific gravity 1.017, albumin 2 per cent, endothelial cells 3.4 per cent, neutrophils 1 per cent. Bacteriologic report: One colony of *Staphylococcus albus* (considered a contamination).

On October 29, the left chest was tapped, it was thought best to remove only eight ounces because the fluid had been in the chest so long. Small amounts were to be taken out at intervals so as to encourage expansion of the lung. Report of the chest fluid: Pale yellow, straw-colored without clot, specific gravity 1.017, albumin 1.7 per cent. Smear of sediment showed a predominance of lymphocytes. Lymphocytes 55 per cent, endothelial cells 4.4 per cent, polymorphonuclear cells 1 per cent.

On November 3, eight ounces of fluid were removed from the left chest, there seemed to be no return of fluid after the last tapping. Breathing was easier. Skin tuberculin reaction, November 6, was strongly positive. On November 7, the left chest was again tapped and about eight ounces of fluid were removed. Immediately afterward, the abdomen was tapped in the right flank and 15 pints of fluid were removed. The girth of the abdomen after tapping was 88.5 cm.

On November 10, there was apparently less fluid in the chest. There was resonance to the third rib in front and midscapula behind. Breathing over this area was as good as on the unaffected side. There was a right border of cardiac dullness 4 cm to the right of the median line.

The left chest was tapped, November 12, and eight to ten ounces of fluid were removed. Ascites increased and was associated with edema of legs. Chest signs remained unchanged. The patient was started on catharsis and diuresis, November 20, to see if the ascites would diminish. The girth of the abdomen was 108 cm. The abdomen was tapped, November 21, and 18 pints were obtained. On November 28, the girth of the abdomen had increased to 103.5 cm, and the patient had gained four pounds in weight in 24 hours. Vaginal examination at this time showed a mass filling the pelvis, crowding the cervix behind the pubes, continuous with the suprapubic tumor.

The tumor was very hard, irregular, nonelastic and in the median line. Operation was advised to relieve a suspected tuberculous condition of the peritoneum and for diagnosis of the uterine tumor.

On December 5, there was so much discomfort caused from the abdominal distention that it was tapped and 260 ounces of fluid were obtained, similar in character to that previously rumored. On December 8, the left chest was tapped and nearly two quarts of fluid were obtained. It was hoped that this would give the lung a better chance to expand.

Operation was performed, December 12. A two-inch median incision was made. The peritoneum was opened, and several quarts of a thin yellowish-brown fluid escaped. A solid ovarian tumor was then delivered with some difficulty, and was removed. Gauze was packed into the pelvis. The pedicle arising from the left broad ligament was tied off with silk and the ovary of that side removed. The abdomen was explored and nothing else abnormal was found.

The pathologic report showed a solid tumor occupying the region of the ovary, measuring about 20 cm in diameter, flattened, and upon section having a white, fibrous surface with some areas slightly hemorrhagic in character. Microscopic examination showed a growth of fibrous tissue with rather numerous and large cells, traversed by vessels having a wall slightly differentiated from the surrounding tissue. A diagnosis of fibroma was made.

Following operation the patient continued to improve, but on December 31, she complained of sharp pain, on inspiration or coughing, in the right axilla. She was transferred to the Medical Service for further observation and treatment. Examination of the heart showed apex impulse not seen but felt faintly in fifth space $8\frac{1}{2}$ cm to the left of the midsternum 2 cm inside the nipple line. Sounds were regular and of good quality. No murmurs were heard. The pulmonic second sound was greater than the aortic and not accentuated. The pulses were synchronous, equal, regular, and of fair volume and tension. The abdomen was slightly rounded, soft, and tympanic throughout. There were no masses or tenderness. The liver was at the sixth rib to the costal border, the edge was not felt. The splenic edge was not felt. There was no edema.

On January 5, 1909, friction rub and pain in the side were still present, but aside from this the patient felt better and was up and about the ward all day. Potassium iodide was given, 10 gr three times a day. She coughed a good deal for 24 hours.

On January 9, there was no fluid in the chest. There was a little dulness at the extreme left base posterior, but normal breathing was heard at the base. There was a coarse friction all over the left back below the scapula and in the axilla. The lungs were otherwise normal. She felt very well. There was no pain in her side. The patient was discharged, January 9, 1909.

On November 11, 1935, a communication from the patient stated that she was in good health and very active. Thirteen and one-half years previously ($13\frac{1}{2}$ years postoperatively) she had had to undergo an operation for adhesions of intestines and removal of the appendix and several small tumors. A letter from the surgeon who performed the operation stated that the patient entered the hospital complaining of spotting of blood of two weeks' duration. Preoperative examination showed adhesions about the uterus and a soft, tender mass in the left adnexal region. A preliminary dilatation and curettage was performed, with negative findings. On opening the abdomen dense adhesions were encountered, many loops of the ileum were adhered to each other and to a mass in the pelvis. The uterus was completely buried in adhesions. The left ovary was buried in a mass of adhesions and consisted of numerous follicle cysts and fibrous tissues, it was dissected out, and together with the uterus (which was very slightly enlarged) was removed. Kidneys, liver, gallbladder, and upper abdomen were all palpated and were apparently negative. The specimens were examined grossly, but no sign of any malignancy was noted. The patient made an uneventful recovery.

Case 5—Mayo Clinic Female, age 36, married, para 1, entered the hospital, July 31, 1917, complaining of a prolapsing uterus and "bloating" of the abdomen. After the birth of her child, three years prior to her admission to the clinic, the patient had been confined to bed for three weeks, menstruated considerably at the time, and for two or three weeks had felt a dragging sensation continually. After about one year, she had noticed a prolapse of the uterus, which gradually came down farther until it protruded four or five inches. At the same time, she had noticed bloating of the abdomen, which was diminished but not entirely reduced after urination, which phenomenon had been more evident during the last six months. Appetite poor. She was constipated at times and passed a yellow, mucus-like material with the fecal matter. There had been a foul discharge for five months. During the spring previous to her entry she had experienced sweats and chills, with some coughing and expectoration. She had steadily lost weight and strength, but there was no coughing or expectoration at the time of her admission.

The family history developed no evidence of cancer or tuberculosis. The patient's first menstrual period, at age 12, had been very painful, since then the periods had been regular. The patient had had a child at the age of 32, at which time the labor had been very difficult. Forceps had been used and there had resulted a bad tear.

Physical Examination revealed a blood pressure of 106/96. Examination of the chest revealed dulness and decrease in fremitus, more marked on the left side. The postcervical axillary nodes were slightly enlarged. The heart dropped a beat every six to 20 beats. The abdomen was distended with fluid, and there was tenderness and bulging over the flanks and a central tympany in a supine position, with a fluid wave. There were large masses attached to, and movable with, the uterus. The cervix was soft and dilated, menstrual discharge was present. A catheterized specimen of the urine revealed an occasional red blood cell. Hemoglobin 71 per cent, leukocytes 8,500. Roentgenologic examination of the chest revealed bilateral fluid extending as far as the seventh rib posteriorly.

In view of the latter finding, aspiration of the chest was carried out, August 4, following which the diagnosis of malignancy was raised. Roentgenologic examination after the aspiration showed some improvement in the chest condition.

On August 16, exploration was performed. A large tumor, the size of a child's head, was found, which had the clinical appearance of malignancy, but which the pathologist reported to be benign. There was marked ascites. The ovarian tumor was very adherent, was impacted in the pelvis, and was difficult to remove. The sigmoid flexure was short. The appendix was normal and was not disturbed. No gallstones could be felt. A subtotal abdominal hysterectomy with bilateral oophorectomy and salpingectomy was performed. The final pathologic report showed metritis, chronic salpingitis, and degenerating fibroma of the right ovary.

The patient's convalescence was uneventful and she left the hospital, August 30, 1917.

She returned to the Clinic again in August, 1921, at which time she stated that she had been well since her operation, her appetite was good, and she had gained 50 pounds in weight. She was again seen in September, 1921, at which time the general examination was essentially negative.

Case 6—Mayo Clinic Female, age 53, married, entered the hospital, November 26, 1920, complaining of bloating of the abdomen and some pain between the scapulae. Three years prior to the patient's admission she fell down 22 steps, after which the menses stopped completely and at that time she began to experience pain in the lower abdomen, which was more severe when she attempted to walk. Associated with this pain was considerable bloating, which was very severe at times. Steam-cabinet baths and abdominal massage gave considerable relief. Following an attack of pleurisy in 1915, there had been some substernal pain and moderate discomfort in the interscapular region. There was no evidence of an acid-fast infection, with the exception of

occasional night sweats The gastro-intestinal history was essentially negative, and it was noted that there had been some dyspnea on exertion and occasional nocturia Three years previous to the patient's entry, she had been hospitalized elsewhere and had had 40 ounces of fluid removed from the chest, and seven weeks later, 60 ounces of fluid were removed The patient had been very dyspneic before her first hospitalization and was relieved only by tapping of the chest, with moderate abdominal ascites

Her father had died of arteriosclerosis, in other respects the family history was essentially negative She had been married 22 years but had never been pregnant Menstrual periods had been normal until three years prior to her admission, at which time they had ceased completely She had had diphtheria several years previously, influenza in 1898, and pleurisy in 1915

Physical Examination revealed a blood pressure of 108/80 An area of dullness to flatness was noted in the lower right chest, no breath sounds were noted, there was an absence of tactile fremitus, whispered pectoriloquy was observed and increased vocal fremitus, amounting to bronchophony The left border of the heart was just within the anterior axillary line, in all probability displaced and only slightly hypertrophic The abdomen was dome-shaped, with signs of the presence of considerable fluid

Uranalysis was essentially negative Hemoglobin 73 per cent, red blood cells 4,600,000 and leukocytes 6,000 Roentgenologic examination of the chest showed fluid in the right chest up to the level of the second rib A paracentesis was performed, November 30, 1920, and six and one-half liters of clear, straw-colored fluid were aspirated On December 1, 1920, about 1,600 cc of clear, straw-colored fluid were aspirated from the right chest, bacteriologic studies revealed no bacteria and no growth of organisms

Abdominal exploration was carried out, December 9, 1920, through a midline incision Several liters of straw-colored fluid were evacuated A large, nodular, friable tumor (about the size of a large grapefruit) of the right ovary was found attached by a rather small pedicle, which was removed The left ovary was about the size of a buckshot and was not disturbed The uterus was normal in size and position There was apparently no metastasis to the peritoneum or liver

Pathologic examination showed an edematous, degenerating fibromyoma, with the remaining ovarian tissue flattened out over it

Convalescence was essentially without incident, and she was discharged, January 14, 1921

Five months later (June 21, 1921), the patient returned to the Clinic She had gained 20 pounds in weight, and her general health was excellent Abdominal and bimanual pelvic examination failed to reveal any trace of recurrence of the tumor

Case 7—Leo⁵ Female, age 64, was admitted to the hospital, March 25, 1926, complaining of dyspnea, cough, and pain in the right chest of several months' duration

Physical Examination revealed a poor general condition, signs of a large pleural effusion in the right side of the chest, and a mass, the size of an adult's head, in the lower part of the abdomen

Repeated chest taps were necessary to keep the patient comfortable, 1,000 cc of fluid being removed every three or four days This had the characteristics of a transudate and no definite diagnosis could be made by study of it Tuberculin skin test was positive Echinococcus skin test was negative Shortly after admission, ascites developed and became quite marked The patient ran a slightly elevated temperature

Because of the downhill course of the patient and because of the apparent hopelessness of the situation, operation was performed, July 25, 1926 The abdomen was opened and a large amount of greenish-yellow fluid escaped A large mass was found occupying the region of the left ovary The uterus, the right ovary, and the other abdominal organs were normal, although no specific mention of the liver was made The mass, which proved to be a benign tumor of the ovary, was removed

After a stormy postoperative period, the patient finally recovered and was dis-

charged on the twentieth day after operation. There had been no return of the fluid except for the withdrawal of 300 cc of fluid from the right chest on the fifteenth day postoperative. No further chest taps were required.

On check-up, two months after discharge, the patient's general condition was excellent, and there was no evidence of fluid in either the chest or abdomen.

Case 8—de Rouville,¹¹ *et al*. Female, age 58, widow, para 4, was admitted to the hospital in April, 1928. The patient was very emaciated and had an enormous abdomen. One year before admission, she had "grippe" for three months, and this was accompanied by a productive cough. The "grippe" apparently over, the patient noticed an increasingly rapid enlargement of her abdomen, without pain. At the end of one month, she had an abdominal tap and 15 liters of hemorrhagic fluid were obtained. Seven other taps were performed within the next eight months. The fluid, always quite abundant, ceased to be hemorrhagic, and gradually became yellow. The general condition changed, almost bordering that of cachexia. Marked dyspnea was present.

Physical Examination showed a very distended abdomen. The puboxyphoid distance was 57 cm, and palpation gave a sense of resistance. Definite fluctuation was present. Percussion elicited the signs of free fluid. Vaginal examination revealed the signs of fluid in the culdesac. No tumor was felt. There was dullness over the left lung with a pleuritic rub over the apex. On exploratory puncture a little yellow fluid was aspirated. On the right side, there was nothing except râles at the base. There was a little edema of the legs.

An abdominal paracentesis was performed, May 1, 1928, and 18 liters of fluid were aspirated. After the fluid had been removed, four or five tumors could be felt under the abdominal wall—some above and some below the umbilicus, hard, tender, and freely movable, giving the impression of epiploic tumors. Vaginal examination confirmed the above findings.

Analysis of the ascitic fluid showed a slight lymphatic reaction. Analysis of the pleural fluid showed exactly the same findings. One week later eight liters of fluid were removed.

On May 10, 1928, an exploratory celiotomy was performed under local anesthesia. On opening the abdomen about one liter of yellow fluid escaped and a large multilobulated tumor was found. There were some adhesions of the mesentery which were easily broken up. The tumor was found to originate in the right ovary, and had a narrow pedicle which had been twisted many times. No other tumors were found.

The mass removed was as large as the head of a child and weighed 1,450 Gm. It consisted of a central cavity surrounded by a dense periphery. It proved to be a fibroma rich in fibroblasts, there were no mitotic figures. No characteristics of malignant disease were evident, only those of hyperplasia of the connective tissue.

Convalescence was uneventful, without recurrence of ascites or dyspnea, and the patient was discharged 20 days postoperative.

Case 9—Salmon,¹¹ Hosp No 337,216. Female, age 52, was admitted to the hospital, April 7, 1932. For three months previous to admission she had been conscious of a mass in the lower abdomen which had increased steadily in size. Her chief complaint upon admission was irregular cramps in the lower abdomen of several days' duration not accompanied by any gastro-intestinal symptoms. Temperature 100° F, pulse 74, respiration 22.

Physical Examination—The patient was a fairly well-nourished female who did not appear acutely ill. Signs of fluid were found in the right chest. In the abdomen, a tense, tender, somewhat irregular mass could be felt arising from the pelvis and reaching to the umbilicus. Hemoglobin 78 per cent, white blood count, 9,000, polymorphonuclear neutrophils, 80 per cent, lymphocytes, 17 per cent, monocytes, 3 per cent. Sedimentation time 13 minutes. The urine examination and the Wassermann reaction were negative. The right chest was tapped, and 1,500 cc of amber-colored fluid aspirated. Laboratory examina-

tion of the fluid revealed Specific gravity 1.018, red blood cells, 1,800 per cubic millimeter, white blood cells, 350 per cubic millimeter, lymphocytes, 70 per cent, polymorphonuclear neutrophils, 30 per cent. No organisms were found on smear or culture. No tumor cells were found on centrifugalization. The fluid rapidly reaccumulated and the right chest was tapped again on two occasions, 1,500 and 2,000 cc of straw-colored fluid being removed. Roentgenograms of the chest following the aspiration failed to reveal any abnormality in the lungs or chest wall to account for the effusion. Roentgenologic examination after the second aspiration disclosed a small amount of fluid also in the left chest.

Since no definite conclusions could be arrived at concerning the etiology of the effusion, it was felt that the nature of the pelvic tumor should be investigated. An exploratory celiotomy was, therefore, performed, and about 500 cc of deep amber-colored fluid were found in the peritoneal cavity. A solid tumor of the right ovary, about the size of a large cantaloupe, was removed. The abdomen was thoroughly explored and no other abnormality was found. Convalescence was uneventful except that, on the eighth postoperative day, signs of fluid were detected in the right chest, and 500 cc of serosanguineous fluid were aspirated. The pathologist reported the tumor as "Edematous fibroma with necrosis."

It is now 24 months since the patient was discharged from the hospital. She has had no symptoms and has gained 40 pounds in weight. There are no signs of fluid in either the chest or abdomen. Roentgenologic examination of the chest reveals nothing abnormal.

Case 10—Massachusetts General Hospital. Female, age 52, single, entered the hospital, August 4, 1934, with the complaint of changes in bowel habits and dyspnea on exertion of three months' duration. She had begun to have loose, watery stools containing mucus, three or four times a day. Shortly after the onset of the bowel discomfort she had noticed dyspnea on exertion of three months' duration. This had gradually become more marked, and on May 10, 1934, she was found to have fluid in the right chest. Considerable fluid was aspirated, with marked relief of the dyspnea. Subsequent taps at ten- to 14-day intervals were necessary to keep her comfortable. About two months prior to admission, she had noticed an increase in the size of her abdomen, frequent injections of salyrgan were administered, with some decrease in the size of the abdomen. There was marked decrease in her general strength and vitality. Her family history was negative.

Physical Examination revealed a patient quite ill, with signs of a large pleural effusion on the right side, and a large amount of fluid in the abdomen. Blood pressure 120/76. Heart normal. No edema of the extremities. No enlargement of any of the peripheral nodes. The liver edge was felt, in spite of the large amount of abdominal fluid, nearly down to the umbilicus. Pelvic examination revealed a hard, orange-sized mass in the left vault.

Urine examination was negative other than for the slightest possible trace of albumin and occasional white blood cells. Complete blood examination revealed a fairly marked secondary anemia. Hemoglobin 65 per cent. Red blood count 3,100,000, white blood count 12,000. The differential count was normal other than for 73 per cent polymorphonuclears. The red and white cells were normal except for achromia of the red cells. Repeated sputum examinations were negative. Repeated stool examinations were negative. Non-protein nitrogen 39 mg, serum protein 7.1 per cent, blood chlorides normal. Hinton test negative. Liver function test was normal. Roentgenologic examination of the chest revealed no abnormalities other than the large amount of fluid in the right chest. Gastro-intestinal series and barium enema were negative.

Two days after admission, 2,300 cc of fluid were aspirated from the right chest with a replacement of 1,500 cc of air. The fluid was a typical transudate. Examination failed to reveal the presence of any tumor cells or tubercle bacilli. Guinea-pig inoculation was likewise negative. Routine culture of fluid was negative. Abdominal tap revealed an identical fluid.

An exploratory celiotomy and left salpingo-oophorectomy were performed, August 18, 1934. The peritoneum was normal. The liver was markedly enlarged, the right lobe

extending to the level of the umbilicus. It appeared, however, perfectly normal in appearance and to palpation. A large amount of yellowish fluid was evacuated. The spleen, stomach, intestinal tract and the kidneys were apparently normal. There was a small gallstone in the gallbladder, and the pancreas was normal. A large solid tumor, which filled the pelvis, and which included the left ovary, was removed. The uterus and right ovary were normal.

The pathologic report showed a very large, solid, firm mass 15×7.5×7 cm. Its cut surface was of a mottled yellow and white color with streaks of white crossing it in every direction. There were one or two areas which appeared finely granular. A diagnosis of fibroma was made.

The patient had a particularly smooth convalescence and was discharged three weeks after operation. Six months after discharge, there was no evidence of chest or abdominal fluid by examination and fluoroscopy. The liver was still enlarged, the lower border being felt about halfway to the umbilicus.

A letter, received in April, 1935, stated that a fluoroscopic examination showed a normal condition, and that her physician had said that, if anything, the right side and chest looked better than the left. She was heard from again in December, 1935, and stated that she was feeling perfectly well.

Case 11—Miller¹¹ L. K., female, age 60, single, had been ailing for several years. She had a large abdominal tumor which had caused a great deal of pressure, pain, weakness, and disability. Recently, she had had some fluid in her right chest and her local physician had tapped her two or three times.

Physical Examination showed a frail, thin woman. The heart action was regular but rapid. There was considerable dulness over the right chest but it became more resonant after the thoracentesis. Abdominal examination showed a large, hard tumor extending from the pelvis to the umbilicus.

At operation, July 16, 1936, under spinal anesthesia, a huge, solid tumor of the right ovary was found, which did not, however, look malignant. It was removed together with the uterus and the other ovary. The pathologic report showed the right ovary replaced by a large, solid mass, measuring 18×14×10.5 cm. Its surface was irregularly nodular, grayish-pink in color, and there were numerous subserous dilated veins. The tumor cut firmly and revealed a mottled, granular, reddish-gray surface with small, yellowish necrotic areas. In the central portion of the mass, there was a large multiloculated, smooth-walled cavity containing clear yellow fluid. A diagnosis was made of a fibroma of the ovary, follicular cysts of the ovary, endometrial polyp, leiomyoma, and cystic hyperplasia of the endometrium.

In June, 1938, the patient was free of any symptoms suggesting pleurisy with effusion or ascites.

Case 12—Weld¹⁸ I. U., female, age 55, was admitted to the Gynecological Service of the Municipal Hospital, Hartford, August 21, 1936, complaining of swelling of the abdomen. About two months prior to admission, she had first noticed the swelling. She also complained of pain in both kidney regions and a low sacral backache. There was a history of chronic constipation.

The menopause had occurred at 35.

Physical Examination revealed a few coarse râles at the base of the right lung, with diminished breath sounds over the same area. The abdomen was shiny and taut, a fluid wave was elicited. A right inguinal hernia in addition to a herniorrhaphy scar was noted. Vaginal examination showed a large, hard, irregular mass filling the pelvis, reaching to two fingers' breadth below the umbilicus, immovable, with tenderness in the region of the sigmoid and rectum. The mass filled the posterior culdesac.

Roentgenologic examination of the chest the day after operation showed no evidence of tuberculosis, but there was increased density at the outer and lower portions of the right lower lobe, with irregularities of the diaphragm and partial obliteration of the costophrenic angle—all indicative of pleural exudate. Blood pressure 112/68. Blood

Wassermann and Kahn tests gave a two plus reaction. Blood nonprotein nitrogen 35.9 mg per cent. The red blood cell count 4,030,000, with 85 per cent hemoglobin.

At operation, about 3,500 cc of straw-colored fluid were removed from the peritoneal cavity by suction. A solid ovarian tumor 9 cm in diameter, together with a multilocular cyst, was removed. The lower pelvis was then found to be filled with a second ovarian tumor, so situated that it predisposed to sigmoidal and rectal obstruction, it was delivered from the pelvis with some difficulty and was removed. Both tubes were then removed, and a supracervical hysterectomy performed. No lymph nodes were found in any part of the peritoneal cavity, nor was there any evidence of extension of the tumor masses to the bowel. There were no bowel adhesions. Each tumor apparently arose from an ovary. Grossly, the tumors appeared smooth and nodular, on section they were composed of dense, gray strands of fibrous tissue. Microscopic sections of the solid tumors showed typical fibromata, no anaplasia and no malignancy. In one or two areas, the pathologist reported the cells to be somewhat large and slightly hyperplastic. The cyst was lined by low epithelium, which, in focal areas, was thrown into a papillary arrangement. Here again, there was no evidence of malignancy.

The patient had an uneventful convalescence and was discharged on the seventeenth postoperative day. Roentgenologic examination of the chest, November 30, 1936, three months after operation, "showed no evidence of pleural effusion." An examination in October, 1938, showed the pelvis to be free from any masses, and there was no evidence of fluid in either cavity.

Case 13—Weld¹⁸ E, female, age 50, married, was admitted to the Gynecological Service of the Hartford Hospital, September 15, 1936, complaining of progressive enlargement of the abdomen of six weeks' duration, and of difficulty in voiding for a relatively short time. During the previous six weeks, she had experienced lower abdominal pain, characterized as a heavy dragging sensation. Menopause occurred ten years prior to admission, and since then there had been no bleeding.

Physical Examination revealed a general appearance of illness, two lipomata on the back, signs of fluid in the right posterior chest, slight enlargement of the heart to the left, an elevated pulse rate, and a pelvic mass rising to the umbilicus, which gave the findings compatible with encapsulated fluid. Stereoscopic and lateral roentgenologic examination of the chest showed "A moderately large amount of fluid in the right pleural cavity, extending into the interlobar fissures and apparently encapsulated in the axilla. The possibility of an underlying pathologic change in the right pulmonary field cannot be excluded without further examination made after a thoracentesis. The left lung is negative in appearance."

An operation was performed under spinal anesthesia three days after admission. The abdomen was opened through a lower midline incision, and was found to be filled with blood-tinged fluid. A solid, right ovarian tumor, with loops of bowel adherent to it, was visualized. The liver was smooth, and normal to palpation. There was no sign of malignant metastases. The uterus, left tube and ovary appeared normal. Only the tumor was removed.

Pathologic Report—Gross "Nodular mass, 15x12x11 cm, encapsulated. On section, it is composed of interlacing strands of rather soft fibrous tissue, through which there are extensive interstitial hemorrhages and dilated vessels. Over one surface is what appears to be a vessel containing blood clot. At one pole of the nodule there is a cyst three centimeters in diameter, having a ragged, seminecrotic lining. *Microscopic* Multiple sections through the nodule show a rather cellular fibrous tissue proliferation. There are some mitotic figures, a few are not entirely regular. There are extensive areas of myxomatous degeneration, and large vascular spaces are scattered through the tissue, in some of which thrombi are present. Structure is fairly characteristic of a benign fibroma of ovarian stroma. *Diagnosis* Fibroma of the ovary."

The patient was discharged on the nineteenth postoperative day, after an uneventful convalescence. Roentgenologic examination of the chest at that time showed less fluid

FIBROMA OF OVARY

than prior to operation. Roentgenograms of the chest seven months after operation showed no evidence of effusion.

Case 14—Macomber⁷ Female, age 32, single, entered the hospital, January 7, 1937. Three years previously, her abdomen began to enlarge and this continued steadily without discomfort or inconvenience until recent months. Being a Christian Scientist, she had not consulted a physician until a short time before admission. About one month previously, the swelling had reached such proportions as to interfere with walking, and she began to have marked dyspnea. This came on quite suddenly and was very severe for one week but then continued with less severity. There was no chest pain other than a feeling of soreness retrosternally. Four months, and again two months, before entry she noticed a small hole just below the umbilicus which discharged fluid for several days. No bowel or urinary symptoms. Catamenia always somewhat irregular but she continued to have menstrual periods during the present illness, the last few more profuse. She has never vomited. On a few occasions she had a sudden breath-taking pain when lying on her left side. No swelling of ankles at any time. There was no cough, sputum, or hemoptysis at any time. Nine years previously, she had several episodes of severe pain in her left lower quadrant. She believes she had lost a good deal of subcutaneous fat but had gained ten pounds, which she attributed to the abdominal fluid.

Physical Examination showed a somewhat thin woman. Heart apparently normal. The patient was obviously cachectic, probably somewhat anemic. The right chest contained fluid. The whole abdomen was tremendously enlarged, and was filled with fluid, it also showed some evidence of containing irregular masses. Rectal examination was practically negative. Roentgenologic examination showed fluid in the chest and abdomen, with displacement of the bowel and fixation of the left side of the diaphragm, probably due to tumors, consistent with adenocarcinoma of the ovary.

On January 9, 1937, the patient's abdomen was tapped, and 292 ounces of fluid obtained. On January 11, 1937, the chest was tapped, and 32 ounces of fluid aspirated. The abdominal fluid showed a specific gravity of 1.016. Differential count showed lymphocytes 19 per cent, polynuclears 2 per cent, monocytes 3 per cent, red blood cell count 18 per cent. The chest fluid showed 1,520 cells per 1/16 square mm. Differential could not be identified by smear. Very slight sediment was found and the fluid was straw-colored. No tumor cells could be identified. A day or two after this, she developed "acute bronchitis" and she was discharged in order to recuperate before operation was undertaken. Her abdomen continued to fill up, and her chest was again tapped at home, February 7, 1937.

The patient was readmitted to the hospital, February 14, 1937, for operation. Under spinal anesthesia, February 15, 1937, a left oophorectomy was performed. The abdomen was opened through a 12-inch median incision. An umbilical hernia was dissected out. No adhesions were found. About two quarts of clear fluid evacuated. The tumor proved to be a fibroma of the left ovary, the size of a rather large full term uterus, filling the entire abdomen, showing a certain amount of cystic degeneration, and weighing about 25 pounds. The tumor was removed. Section proved it to contain a cavity containing about two quarts of fluid. Some of the fluid was lost in removal. No obvious evidence of malignancy was seen. The uterus seemed normal, there were no peritoneal implantations. A normal tube and ovary and small uterus were left.

No acid-fast bacilli found in the sputum, which was examined, February 20, 1937. Roentgenograms of the chest, February 27, showed that the fluid in the left side of the chest had completely disappeared. There was a haziness at the left base, apparently due to thickening of the pleura. The patient had an uneventful convalescence and was discharged, March 6, 1937.

The pathologic report showed a rounded, smooth, grayish, firm, previously opened mass, measuring 25x22x18 cm. Through the grayish capsule could be seen several darkish, cystic areas, which on section were previously opened cysts containing clotted blood. The lining membrane was grayish, smooth, and glistening. The central portion

was made up of multilocular cysts, the largest measuring 15x9x7 cm. The grayish, firm tissue presented a smooth, glistening, firm surface. A diagnosis of a degenerated fibroma was made.

On June 28, 1937, the patient was seen and the scar was solid. Air passed well to bases of lungs. She had gained 12 pounds since April, 1937.

Case 15—Rhoads and Terrell¹² E. P., female, age 57, widow, para 3, was admitted to the hospital of the University of Pennsylvania, in the service of Dr. Alfred Stengel, February 1, 1937, complaining of shortness of breath, fatigue and the loss of 18 per cent of her body weight.

Her symptoms were first noticed in 1933, and had grown gradually worse. Dyspnea, at this time, developed when she ascended one flight of stairs, or merely with excitement. When she became dyspneic, a dry cough developed, but she had never had hemoptysis or pain in the chest. Palpitation had been noted during attacks of dyspnea and fatigue. She had never observed any peripheral edema. There were no digestive symptoms except for moderate anorexia and belching. She had never had any abdominal pain nor had she ever complained of abdominal fullness or distention.

The menopause occurred at age 53, four years before the present admission. The menses had begun at age 15, and had always been regular. There had been no post-menopausal bleeding or discharge. For many years, the patient had been under the care of a physician, who had noted a large pelvic tumor in the median line, at least eight years previous to her admission, which had not grown appreciably during the interval.

Physical Examination—The patient was thin and rather cachectic looking and was prematurely aged. Examination of the chest revealed signs of a massive pleural effusion on the right side. The trachea was deviated somewhat to the left and the apex of the heart was displaced toward the left. There were no other abnormal physical signs in the left side of the chest. These observations were confirmed roentgenologically. Abdominal examination indicated the presence of a small amount of ascites. In the right upper quadrant, the liver was palpable three fingers' breadth below the costal margin. A large, round, firm tumor extended from the pelvis to a point midway between the symphysis pubis and the umbilicus. On pelvic examination this appeared to be attached to the cervix, it was firm, freely movable with the uterus and not tender. The pelvic mass prevented satisfactory palpation of the adnexa. There were no nodules felt in the culdesac. Temperature 98° F, pulse 90, respiration 20, blood pressure 130/85. Because of the ascites and hydrothorax, a tentative diagnosis of uterine sarcoma with metastases was made.

Thoracentesis was performed five times. The fluid removed from the right pleural cavity amounted to February 2, 1,900 cc, February 5, 1,000 cc, February 10, 3,000 cc, February 19, 2,000 cc, and March 3, 1,000 cc. One and one-half liters of air were injected in an attempt to obtain better roentgenographic visualization of the pleura and right lung field. Within nine days, roentgenologic examination of the chest showed a reaccumulation of a large amount of fluid. So rapid was this reaccumulation, that there was a large mediastinal herniation, containing both air and fluid, which extended to the midportion of the left lung field. This necessitated removal of 2,000 cc of fluid, for relief of the dyspnea.

Laboratory Data Red blood cells 5,500,000, white blood cells 18,200, hemoglobin 98 per cent. Polymorphonuclear cells 75 per cent, lymphocytes 22 per cent, monocytes 2 per cent, eosinophils 1 per cent. Subsequent blood counts never disclosed a leukocytosis. Repeated urinalyses showed a specific gravity varying from 1.012 to 1.027, an occasional trace of albumin and a moderate number of white blood cells. The Kolmer and Kahn tests were negative for syphilis. The urea nitrogen content of the blood 15 mg per 100 cc. Serum protein determination was 6.9 Gm per 100 cc. Sedimentation rate 22 mm in 60 minutes.

The pleural fluid obtained, February 2, showed a specific gravity of 1.021. It contained 450 cells per cubic millimeter (96 per cent mononuclear and 4 per cent poly-

morphonuclear) and 1.75 Gm of protein per liter. February 5, fluid with similar specific gravity showed, on long centrifugation, only an occasional normal red blood cell and a few lymphocytes and polymorphonuclear cells. No mitotic cells were found. None of the cells appeared malignant. February 19, the specific gravity was 1.014, the protein was 1 Gm per liter and the cell count was 514 cells, with 86 per cent mononuclear and 14 per cent polymorphonuclear cells. Cultures of the fluid were repeatedly negative, guinea-pig inoculation was made on two occasions, but tuberculosis did not develop in the animals.

TABLE III

Ages	33-64
Status	
Single	4
Married	9
Unknown	2
Fertility	
Children	6
No children	5
Unknown	4
Location of tumor	
Left ovary	4
Right ovary	6
Both ovaries	2
Unknown	3
Taps	
Abdominal	6
Chest	12
Location of effusion in thorax	
Left side	3
Right side	10
Both sides	1
Unknown	1

Because numerous roentgenologic examinations following injections of air did not show the expected pleural or pulmonary metastatic lesion, thoracoscopy was considered. It did not offer the patient much prospect of benefit, however. At this time the gynecologic consultant, Dr. Franklin Payne, suggested that the pelvic tumor might be an ovarian fibroma, and be presenting the syndrome described by Meigs and Cass.¹⁰

Accordingly, March 4, 1937, an exploratory celiotomy was performed by Dr. I. S. Ravdin. A moderate amount, probably in excess of 750 cc of ascitic fluid, was evacuated. The pelvic mass proved to be a tumor of the right ovary, measuring 14x10.5x10 cm. It was readily removed. Exploration of the remainder of the peritoneal cavity showed no abnormalities. Convalescence from operation was smooth and uneventful. The last pleural aspiration was performed on the day before operation, when 1,000 cc of fluid were removed.

Roentgenograms of the chest, taken on the sixth and fifteenth postoperative days, showed progressive diminution in the pleural effusion and reexpansion of the right lung. The patient did not require thoracentesis following the operation. At the time of discharge, March 23, 1937, the blood count was entirely normal, the serum protein was 7.3 Gm per 100 cc, and the patient was subjectively cured and objectively improved.

Follow-up examination, April 22, 1937, seven weeks following operation. The patient was feeling very well, an excellent appetite had replaced the anorexia, she had no

symptoms of breathlessness, cough or fatigue, and she had gained weight. Physical examination was negative except for the signs of a very small amount of fluid or thickened pleura at the right base. Roentgenologic examination at this time showed great improvement in the appearance of the right lung field. The entire right lung had reexpanded, and there was only a small amount of fluid above the dome of the diaphragm. The pleura appeared somewhat thickened.

TABLE IV

FINDINGS AT OPERATION

Case No	Fluid	Amount	Adhesions	Size	Position
1	?	Large quantity (autopsy)	No	12 cm 15 cm	Both ovaries
2	Straw	Considerable	Yes	20 cm	Ovary
3	Clear	6 to 8 quarts	Yes	14 cm	Right ovary
4	Yellow-brown	Several quarts	Yes	20 cm	Left ovary
5	Ascitic	Marked	Extreme	Child's head	Ovary
6	Straw	Several liters	Doubtful	Grapefruit	Right ovary
7	Green-yellow	Large amount	Doubtful	Large	Left ovary
8	Yellow	1 liter	Yes	Child's head	Right ovary
9	Deep amber	500 cc	?	Large cantaloupe	Right ovary
10	Yellowish	Large amount	?	15 cm	Left ovary
11	?	? (fluid in abdomen)	?	18 cm	Right ovary
12	Straw	3,500	No	9 cm	Both ovaries
13	Blood-tinged	?	Yes	15 cm	Right ovary
14	Clear	2 quarts	No	25 cm	Left ovary
15	Ascitic	750 cc	?	14 cm	Right ovary

TABLE V

Case No	Entered Hospital	Operation	Follow-Up
1	March 11, 1879	Died without operation	September 10, 1879 (died)
2	April 29, 1901	September 20, 1901	December, 1902
3	June 9, 1902	June 10, 1902	October 25, 1913 (died)
4	October 9, 1908	December 12, 1908	November 11, 1935
5	July 31, 1917	August 16, 1917	September, 1921
6	November 26, 1920	December 9, 1920	June 21, 1921
7	March 25, 1926	July 25, 1926	October, 1926
8	April, 1928	May 1, 1928	?
9	April 7, 1932	?	April, 1934
10	August 4, 1934	August 18, 1934	December, 1935
11	July 16, 1936	July 16, 1936	June, 1938
12	August 21, 1936	August, 1936	November 30, 1936
13	September 15, 1936	September 18, 1936	April, 1937
14	January 7, 1937	February 15, 1937	June 28, 1937
15	February 1, 1937	March 4, 1937	April 22, 1937

Pathologic Examination—The tumor weighed 80 Gm. It was rounded and smooth. The surface was traversed by a few moderately large vessels. The consistency was firm, approximately that of a squash ball. The tumor appeared to be a diffuse enlargement of the ovary. On section, it showed whorls of fibrous tissue such as those often seen in uterine fibromyomata. No cystic areas were found. Sections were cut at right angles to the surface and stained with hematoxylin and eosin. The tumor appeared to be composed of fibrous tissue with numerous fibroblasts. This was interspersed, in every

low power field, with eosin-staining areas having the appearance of smooth muscle. The Masson stain, which colors fibroblasts purple and muscle cells green, definitely established the presence of both elements. The pathologic diagnosis was stromatogenous fibromyoma of the ovary.

DISCUSSION —The problem of why fibromata of the ovary may be accompanied by fluid in the chest and abdomen is so far unsolved. Various suggestions have been made and valid objections have been brought against each. The most obvious suggestions are anatomic or changes in the body chemistry. The work of St. Karady, Browne and Selye¹⁷ on the "alarm reaction" must be discussed. Let us consider the anatomic features first. In the two-month-old human embryo the abdominal and pleural cavities connect. Later, this connection is broken by the presence of the diaphragm. Malformations of this broad muscle do occur and there are diaphragmatic herniae without sacs, where free communication exists between the abdomen and chest. In the event of a defect of this type in a woman with a fibroma of the ovary and with fluid in the abdomen, fluid would also be expected to be found in the chest. But that this rare anatomic anomaly could explain all cases in this rare syndrome does not seem probable. Drainage of either cavity in such an anatomic set-up should drain the other cavity, and this does not occur. Large diaphragmatic herniae are not uncommon and a sac is usually present. It is not possible to see how such a lesion could account for chest fluid except that abdominal fluid might fill the sac. An abdominal paracentesis should drain the chest and yet it does not. Small openings in the diaphragm can be conceived of, but their rarity and the unusualness of this condition rule out the possibility. It is difficult to believe any anatomic lesion is responsible for this syndrome.

An explanation on a chemical basis (protein deficiency) is a distinct possibility, but in only two cases have determinations of the serum protein been made. In both cases, the serum protein was found to be within normal limits—71 mg in Case 10, and 69 mg before operation in Case 15 and 73 after operation. In neither case was the serum albumin-serum globulin ratio known. It is interesting to note that three patients had very moderate peripheral edema of the legs. It is difficult to believe that protein deficiency can account for massive effusion and ascites without more evidence of peripheral edema. One can conceive of changes in the serum protein after multiple withdrawals of fluid, but this does not explain the original cause of the fluid. A circulatory phenomenon affecting capillaries and lymph vessels, with stasis sufficient to produce pleural effusion and ascites, should be accompanied by peripheral edema. Shock, with changes in blood volume and peripheral vasoconstriction and tissue edema, does not offer an explanation for the two large collections of fluid.

The "alarm reaction" of Selye with accumulations of pleural and peritoneal fluid is a constant finding when animals are exposed to damaging agents. Doctor Selye writes that "this was particularly obvious in cases in which irritating substances had been introduced into the peritoneal cavity." He considers it possible that "the fibroma might have acted as an irritating agent and that the

accumulation of pleural fluid was a direct result of the ovarian tumor." In this experimental work in animals (rats) it has been shown that repeated minor traumata cause a resistance to be built up and the appearances and functions of the organs return practically to normal. After a period of one to three months, with continued injury, the animals lose their resistance and succumb with symptoms similar to histamine toxicosis or surgical or anaphylactic shock plus accumulations of a peritoneal and pleural transudate. It is possible then to think of the fibroma as an irritating and shocking agent. At some time in the patient's life a general adaptation to continued injury is brought about, but later, due to its continued presence, a chronic form of "general alarm" phenomena sets in.

Selye's "alarm reaction" appears to the author to be the most satisfactory explanation so far for the presence of the fluid, but it must be admitted that this is not perfect.

Other pelvic lesions of a benign type may cause this syndrome, for instance, U J Salmon,¹¹ in 1934, reported a patient with a large fibroid uterus with some intraligamentous development who had sanguineous fluid in the right chest and abdomen. Seventeen months after operation, careful study revealed no evidence of residual disease or fluid. In the discussion of Meigs and Cass's¹⁰ paper in 1937, W T Danneuthner presented a patient with a benign ovarian cyst who had fluid in her chest and later, after the operation, the fluid completely disappeared. It is possible, therefore, that there are other benign tumorous conditions in the pelvis besides fibroma of the ovary which may be accompanied by ascites and hydrothorax.

CONCLUSIONS

(1) Fifteen cases of fibroma of the ovary with ascites and hydrothorax are presented.

(2) In spite of increasing interest in the subject, no adequate explanation of either the ascites or hydrothorax has been suggested.

(3) The "alarm reaction" of Selye offers a better explanation than anatomic or chemical ones.

(4) The importance of this syndrome to patients suspected of some fatal disease is obvious. More search should be made in patients considered to have metastatic cancer for this benign entity.

(5) The possibility of this syndrome should always be in the mind of the internist and surgeon.

Thanks are due to many who have willingly helped and discussed this problem with me. I especially wish to acknowledge my indebtedness to Drs Edward Churchill, Leland S McKittrick, Isidor Ravdin, U J Salmon, Donald Macomber, Richard H Miller, Peter Gruenwald, Cecil Drinker and J S L Browne.

REFERENCES

- ¹ Cullingworth, C J. Fibromas of Both Ovaries. Trans. Obst. Soc. of London, 21, 276, 1879.
- ² Case Records of the Massachusetts General Hospital. Fibroma of the Ovary (Cabot, Case No 21411). New England Jour. Med., 213, 723, 1935.

- ³ Frank, Robert T Review of Stoeckel's Handbuch der Gynakologie, Vol 7 Amer Jour Obstet and Gynec, 31, 1059, 1936
- ⁴ Hoon, Merle R Fibromata of the Ovary Surg, Gynec and Obstet, 36, 247, 1923
- ⁵ Leo, C Processo essudative pleuro-peritoneale ribelle guarito in seguito a laparotomia per tumore ovarico Med Pract, 11, 422, 1926
- ⁶ Lynch, Frank W, and Maxwell, Alice F Pelvic Neoplasms New York, D Appleton-Century Co, 1922
- ⁷ Macomber, Donald Personal communication
- ⁸ McIlrath, Muriel B Fibroma of the Ovary A Clinical Study J Obst and Gynec, Brit Emp, 44, 1102, 1937
- ⁹ Meigs, Joe V Tumors of the Female Pelvic Organs New York, the Macmillan Co, 1934
- ¹⁰ Meigs, Joe V, and Cass, John W Fibroma of the Ovary with Ascites and Hydrothorax Am J Obst and Gynec, 33, 249, 1937
- ¹¹ Miller, Richard H Personal communication
- ¹² Rhoads, J E, and Terrell, A W Ovarian Fibroma with Ascites and Hydrothorax (Meigs' Syndrome) J A M A, 109, 1684, 1937
- ¹³ de Rouville, G, Villa, G, Buibert, H L, and Lafourcade, E Un cas de fibroma de l'ovaire Arch Soc d sc med et biol de Montpellier, 9, 373, 1927-1928
- ¹⁴ Salmon, U J Benign Pelvic Tumors Associated with Ascites and Pleural Effusion J Mt Sinai Hosp, 1, 169, 1934
- ¹⁵ Selye, Hans Personal communication
- ¹⁶ Selye, Hans A Syndrome Produced by Diverse Nocuous Agents Nature, 138, 32, 1936
- ¹⁷ St Karady, Browne, J S L, and Selye, H The Effect of the Alarm Reaction on Water Excretion Quart Jour Exper Physiol, 28, 23, 1938
- ¹⁸ Weld, Stanley B Fibroma of the Ovary with Ascites and Pleural Effusion New England Jour Med, 218, 262, 1938

DISCUSSION—DR WILLIAM F MACFEE (New York) In connection with Doctor Meigs' paper, I should like to mention a case that came to my attention last November. The patient, female, age 54, gave a history of progressive enlargement of the abdomen for a period of one year. During that time she noticed a loss of weight from other parts of her body, progressive emaciation, loss of strength, and for about one month she had had very distressing dyspnea which practically disabled her.

Upon admission to the hospital, the positive findings were an enormous enlargement of the abdomen with marked emaciation elsewhere. On percussion, the abdomen was entirely flat throughout. Tympany was absent even over the stomach, and there was all the evidence of fluid in the abdomen.

In addition, the right chest was completely flat to percussion and the breath sounds were absent. The presence of fluid in the chest was confirmed roentgenologically. The chest was aspirated and 1,500 cc of a greenish-brown fluid were removed. Tubercle bacilli could not be demonstrated and nothing except a few lymphocytes and some desquamated pleuritic cells were found.

The patient appeared to be in the final stages of malignant disease of the ovary. With the idea of palliation rather than cure, operation was advised in the hope that removal of the large cyst might afford some relief from her distress.

At operation, a very large cyst was found lying rather free in the abdomen, surrounded by a thin film of free abdominal fluid. The cyst was removed without difficulty, and the patient had a relatively uneventful convalescence. Ten days after operation, however, it was necessary to aspirate the chest once more because of reaccumulation of the fluid. Her course after the second

aspiration was free of further complications. She made a good recovery and is well to-day.

Pathologic examination of the tumor showed it to be a cystic adenoma, multilocular in type, with no evidence whatever of malignancy.

I think the profession owes a great deal to Doctor Meigs for calling attention to this condition in which there is fluid in the chest associated with a benign tumor of the ovary. Recognition of this possibility may very well lead to a more careful investigation of cases of this kind, and to the saving of a certain number of patients who otherwise might needlessly die.

DR JAMES C. MASSON (Rochester, Minn.) I think the paper Doctor Meigs has presented is a most interesting one, and the syndrome he has described is something we should all look for. From January 1, 1910, to December 31, 1938, there were 428 cases of ovarian fibroids listed in the records of the Mayo Clinic. In many of the earlier cases no roentgenograms of the thorax were made, and it is impossible for me to speak definitely about small collections of fluid in the thorax, because such a condition was mentioned in only two instances.

This syndrome is an important point to keep in mind when patients having ascites and pleural effusion are seen. There is no doubt that in the past all such patients were considered to have a malignant process, and most of them refused surgical treatment. No doubt the patient in an occasional case in which the collection of fluid is due to this benign condition is refused surgical treatment at a time when a relatively safe operation would be possible.

Ninety-one patients for whom a postoperative diagnosis of fibroma of the ovary was made have been encountered at the Mayo Clinic during the last four years. Of the fibromata present in these 91 patients, 23 were 5 cm or more in diameter, and ten were bilateral. Routine roentgenograms of the thorax were made in practically all of these cases before operation, and in no instance was the presence of fluid noted, but from a small amount to several hundred cubic centimeters of fluid were noted in the abdomen in a great many cases. Just why a few of these tumors cause fluid to accumulate in the thorax as well as in the abdomen (and a great majority do not) is hard to explain.

It happened that since I was first asked to discuss this paper I have operated upon two cases of fibroma of the ovary. Both of these tumors were about the same size (15x12x10 cm). Very marked fatty degeneration was present in the first one, which originally was a typical fibroma. A simple cyst was also present in the same ovary. It was hard to recognize any normal ovarian tissue. Several hundred cubic centimeters of fluid were present in the abdomen of this patient, but there was no indication of any change in the thorax.

The patient's history in the case involving the second fibroma was practically the same as that for the first patient, but I suspected the possibility of the presence of malignancy in this woman, and I therefore did a total hysterectomy, removing the left ovary as well, and in it was found another small fibroma.

I think that Doctor Meigs has drawn attention to a very important condition, and I am satisfied that if all surgeons are on the alert for this syndrome and advise operation in cases in which there is not a definite proof of metastasis in the thorax, more of these cases will be discovered.

DR JOE VINCENT MEIGS (closing) I hoped somebody from the Presbyterian Hospital would say something, because I heard last week, when in New York, that they had had a patient there who had died, in whom they found fluid in both the abdomen and chest. At autopsy, a fibroma of the ovary was found. I feel there must be many more cases, and I think in the future they probably will be reported.

THE EFFECT OF DISTENTION OF THE COLON AND STIMULATION OF ITS NERVE SUPPLY ON THE FLOW OF BILE FROM THE LIVER*

LEON GOLDMAN, M S , M D , AND A C IVY, P H D , M D

CHICAGO, ILL

FROM THE DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO, ILL

STASIS OF BILE is considered an important factor in the etiology and symptomatology of cholecystic disease or malfunction. When present, certain chemical changes in the gallbladder bile take place¹ which may influence the formation of calculi. Although it is well known that physiologic or pathologic disturbances of the biliary system may inhibit the flow of bile,² there is also evidence to show that changes elsewhere in the body may cause a similar effect.

The gallbladder of pregnant women have been found to be more distended³ and their emptying times more prolonged than normal.⁴ This delay in evacuation may be due (a) to the action of the sex hormones of pregnancy, (b) to a reflex inhibition of bile formation, (c) to reflex inhibition of the gallbladder, (d) to a reflex contraction of the sphincter of Oddi or the choleododuodenal mechanism, and (e) to metabolic changes in the chemistry of bile. Biliary stasis during the latter part of pregnancy is associated with a low bile salt and high cholesterol content in the gallbladder bile, thereby favoring the precipitation of cholesterol out of solution.⁵ Its presence may partially explain the symptomatology referable to the organ during pregnancy and the high incidence⁶ of cholecystic disease afterwards.

The occurrence of constipation during and after pregnancy is well known. Blalock⁷ has reported it as a symptom of gallbladder disease in 62 per cent of 735 patients in whom gallbladder disease was proven at operation. The incidence of cholecystopathy has been found to be doubled in patients with diverticulosis of the colon⁸ and in patients with peptic ulcer or recurring appendicitis.⁹ Boyden and Buch¹⁰ have shown that stimulation of the duodenum, jejunum and cecum in animals inhibits evacuation of the gallbladder. Many observers¹¹ have reported a high incidence of irritable colon in patients with organic cholecystitis, biliary dyskinesia or abnormal visualization by cholecystography. Lahey and Jordan¹² have observed improvement of the gallbladder shadow in 44 of 65 patients, who had absent or faint roentgenologic visualization after their irritable colon was treated a short period. Kunath,¹³ in discussing the symptomatology of the stoneless gallbladder, suggests that a spastic biliary tract might accompany a spastic intestinal tract. Proper management of constipation or irritable colon, when present, often ameliorates the symptoms referable to the biliary tract.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

The foregoing evidence indicates the possible existence of a causal relationship between abnormal function of the colon and cholecystopathy. Disturbances of the colon might predispose to cholecystopathy (a) by reflexly inhibiting the flow of bile from the liver, (b) by reflexly causing hypertonicity of the sphincter of Oddi and the duodenum, and (c) by reflexly inhibiting the evacuation of the gallbladder. This investigation was undertaken to determine whether stimuli from the colon could reflexly inhibit the flow of bile from the liver.

Methods—The experiments were all of the acute type, performed upon dogs fasted for 18 hours and anesthetized with sodium pentobarbital. The trachea was cannulated and the carotid blood pressure recorded. The cystic duct was ligated near its entrance into the common bile duct and the latter was cannulated close to the duodenum. The drops of bile were recorded on a revolving kymograph by an electrical recorder. It was usually necessary to wait 15 to 25 minutes before a regular control flow was obtained. A ligature was placed about the sigmoid colon just above the pelvic floor and another around the terminal ileum. A large cannula, through which the colon was slowly distended with tap water at 40°C, was inserted into the "appendix" and held in place by means of a purse-string suture. The amount of fluid injected depended upon the size of the dog and varied from 200 to 500 cc. The colon was never distended beyond the stage of compressibility and was permitted to remain distended for a five- to ten-minute period.

The only possible source of technical error in these experiments was the effect of kinking of the common duct at the site of entrance of the glass cannula. The distended colon occasionally angulated the small rubber tube attached to the cannula so as to obstruct the flow of bile. This could always be readily recognized by the presence of an increased flow above the control rate, during or immediately following deflation of the colon. At times it was necessary to gently retract the colon manually to the left side of the abdomen to obviate this possibility. Although this source of error was not as likely to be present while the nerves were being stimulated, it had to be constantly kept in mind.

The central cut end of the nerves was stimulated for a five-minute period with a shielded electrode which received its current from an inductium, the source of electricity being two dry cell batteries. The secondary coil was set at from 3 to 6.5 cm, depending upon the degree of stimulation to the animal and the degree of rise in blood pressure.

Results—*Distention of the Colon* (Table I)—Distention of the entire colon was associated with an inhibition of bile flow in 12 of 14 dogs (Graph 1). The diminished flow ranged from 18 to 80 per cent below the control level, or an average of —48.5 per cent, and was coexistent with a rise in blood pressure from 5 to 30 Mm Hg. Although two dogs showed a normal blood pressure level, distention of the colon produced no change in bile flow in one (Table I, No. 16) and only a diminution of 8 per cent in the other (Table I, No. 10). These results are not significant and are recorded as *not*

EFFECT OF DISTENTION ON BILE FLOW

effective Distention of the distal half of the colon in three dogs and the proximal half in two produced no change in the former group and only a slight inhibition in the latter. This suggests that the proximal is more sensitive than the distal colon.

TABLE I
RESULTS OF EFFECT OF DISTENTION OF THE COLON ON RATE OF BILE FLOW
BEFORE AND AFTER SECTION OF HEPATIC NERVES

Dog No	Distention of Colon			Section Hepatic Nerves			Distention of Colon After Section Hepatic Nerves		
	Control	During†		Control	After‡	Per	Control	During	
	Bile Flow—Cc Per Hour*	Distention—Cc Per Hour	Per Cent Change	—Cc Per Hour	—Cc Per Hour	Cent Change	—Cc Per Hour	Distention—Cc Per Hour	Per Cent Change
2	5 4	3 6	-33%						
3	7 8	5 1	-35%						
4	1 5	0 3	-80%						
5	6 3	2 7	-57%						
6	4 8	1 8	-63%				6 0	6 0	0%
7	7 8	3 0	-64%	4 8	7 2	+50%	6 0	6 0	0%
8	4 2	2 1	-50%						
9	2 7	2 1	-23%	3 6	5 4	+33%	4 5	4 5	0%
10	3 6	3 3	-8%						
11	4 8	4 2	-18%	4 2	6 0	+43%	6 0	5 7	-5%
12	1 5	0 6	-60%				5 4	5 4	0%
16	4 8	4 8	0%						
18	6 6	3 6	-57%						
19	4 8	3 0	-45%				6 0	6 0	0%

* Calculated on basis of ten-minute control period preceding distention

† Calculated on basis of five-minute control period during distention

‡ Calculated on basis of first ten-minute control period after section of hepatic nerves

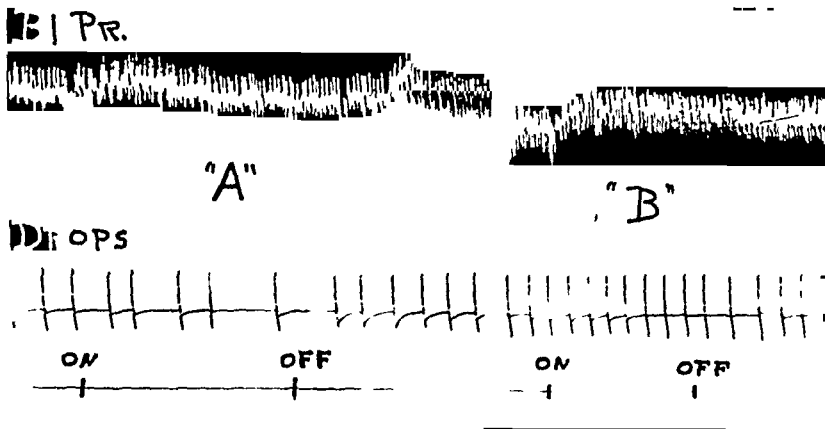
Distention of the entire colon in Dogs No. 4 and No. 18 did not influence bile flow after marked choleresis had been caused by administering 2 cc. of 20 per cent sodium dehydrocholate intravenously. The choleric stimulus of the injected oxidized bile salt was more powerful than the inhibitory effect of colonic distention, a point which should be of therapeutic significance.

In two dogs, the colon was distended after the vagi were sectioned in the neck, and the same inhibition in bile flow took place. This indicates that the reflex pathway is not resident in the vagi.

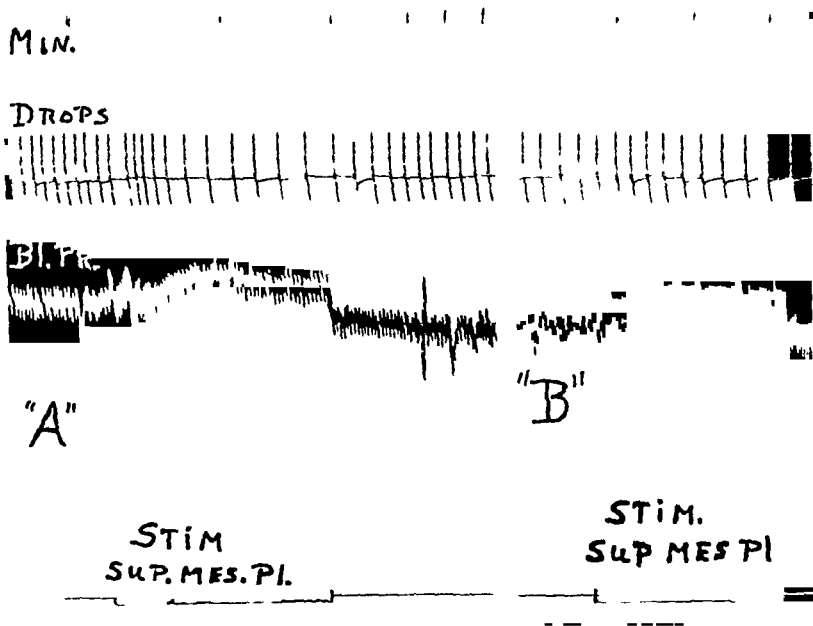
In three rhesus monkeys, the same experiments were carried out in a similar manner and bile formation was uniformly inhibited. Control flows

of 30, 42 and 36 cc per hour were decreased to 20, 30 and 21 cc per hour, or —33, —29 and —41 per cent respectively, averaging —34.4 per cent

Stimulation of the Central End of Colonic Nerve—Stimulation of the splanchnic nerves to the intestinal tract caused a similar inhibition in bile flow from the liver, suggesting that the response from the distention of the



GRAPH 1—Showing the effect of distention of the colon before, "A," and after, "B," section of the hepatic nerves on bile formation



GRAPH 2—Effect of stimulation of the superior mesenteric plexus before, "A," and after, "B," section of the hepatic nerves on bile flow

colon is due to nervous reflex effect upon the liver. The colonic nerve innervates most of the descending colon and can be found in its mesentery accompanying the caudal or inferior mesenteric artery. Stimulation in four dogs (Table II) caused an inhibition in bile flow ranging from —17 to —79 per cent, averaging —37 per cent. Although this represents the period during stimulation in about one-third of the cases, the inhibition persisted for

EFFECT OF DISTENTION ON BILE FLOW

several minutes after the current was interrupted. During the stimulation of the nerves the blood pressure rose from 10 to 80 Mm Hg above the control levels. This pressor effect was more marked on nervous stimulation than on distention of the colon.

TABLE II

RESULTS OF EFFECT OF STIMULATION OF COLONIC NERVE ON BILE FLOW
BEFORE AND AFTER SECTION OF HEPATIC NERVES

Dog No	Stimulation Colonic Nerves			Section Hepatic Nerves			Stimulation Colonic Nerve After Section Hepatic Nerves		
	Control Bile Flow —Cc Per Hour	During Stimulation	Per Cent Change	Control —Cc Per Hour	After Section —Cc Per Hour	Per Cent Change	Control —Cc Per Hour	During Stimulation	Per Cent Change
I	3.6	1.5	-79%	7.2	9.0	+20%	7.2	7.2	0%
17	10.2	8.4	-18%						
19	3.6	2.7	-25%						
24	10.8	9.0	-17%	5.4	6.0	+10%	4.8 3.6	4.2 3.6	-12% 0%
Stimulation Inferior Mesenteric Plexus				Inferior Mesenteric Plexus			Stimulation Inferior Mesenteric Plexus After Section of Hepatic Nerves		
I	3.6	2.4	-33%	6.0	10.2	+62%	6.0 7.2	6.0 7.5	0% +4%
2	3.0	2.1	-30%						
	3.0	1.3	-55%						
5	6.3	3.0	-52%						
19	5.4	2.4	-57%						
	5.4	3.6	-33%						
21	3.6	2.7	-25%	7.2	8.4	+16%	6.3 6.3 4.8 4.2	6.3 6.0 4.8 4.2	0% -5% 0% 0%
22	9.0	6.3	-30%						
23	2.4	1.8	-25%						
26	3.0	2.4	-20%				3.9	4.2	+7%

Stimulation of the Central End of the Inferior (Caudal) Mesenteric Plexus—(A) This group of nerve fibers was sectioned and its central end stimulated with a shielded electrode just cephalad to the juncture where the twigs from the superior hemioithoidal fibers join the colonic nerve. Ten stimulations in eight dogs were associated with a -20 to -57 per cent inhibition of bile flow, or an average of -36 per cent (Table II).

Four stimulations in three monkeys reduced the control flows of 3.6, 3.6,

30 and 30 cc per hour to 24, 27, 24, and 18 cc per hour, or —33, —25, —20 and —40 per cent, respectively, the average reduction being 30 per cent

Stimulation of the Central End of Superior (Caudal) Mesenteric Plexus—(B) This group of nerve fibers supplies the small intestine and part of the proximal colon. They were freed from the superior mesenteric artery in the root of the mesentery of the small bowel divided and enclosed in a shielded electrode. Stimulation of this plexus caused a slowing of from 33 to 53 per cent, or an average inhibition of 38.7 per cent (Chapter 2, Table III), in bile formation.

TABLE III

RESULTS OF EFFECT OF STIMULATION OF SUPERIOR MESENTERIC PLEXUS ON RATE OF BILE FLOW BEFORE AND AFTER SECTION OF HEPATIC NERVES

Dog No	Stimulation Superior Mesenteric Nerves			Section Hepatic Nerves			Stimulation Superior Mesenteric Nerves After Section Hepatic Nerves		
	Control Bile Flow—Cc Per Hour	During Stimulation—Cc Per	Per Cent Change	Control—Cc Per Hour	After Section Hepatic Nerves	Per Cent Change	Control—Cc Per Hour	During Stimulation	Per Cent Change
25	5.4	3.6	—33%	3.6	1.6	+25%	3.0	3.0	0%
							3.6	3.6	0%
32	9.0	4.2	—54%	3.0	4.8	+38%	6.6	6.6	0%
33	3.6	1.8	—50%				6.6	6.0	—9%
34	7.8	4.8	—38%				6.6	6.6	0%

Distention of Urinary Bladder—The urinary bladder was distended in three dogs by injecting 125 to 200 cc of tap water at 40°C (Table IV). An inhibition in bile flow of —30, —40 and —40 per cent, averaging —37 per cent, was observed. It has been noted during many bile-flow experiments that there was usually an acceleration in bile flow during spontaneous micturition, without any associated alteration in blood pressure. This agrees with the observations just mentioned.

Stimulation of the Central End of the Pelvic Nerve—The pelvic nerve was stimulated once in two dogs and twice in two other dogs. A diminished bile flow of from —30 to —45 per cent, or an average of —37 per cent, resulted (Table IV).

Section Hepatic Nerves, Followed by Distention of Colon and Stimulation of Nerves—Nearly all the nerve supply to the liver surrounds the hepatic artery near the hilum and comprises a rich plexus of fibers, which together often almost equals the size of the artery itself. This plexus is made up predominantly of splanchnic fibers which spread from the celiac plexus along

the arterial pathways. It also contains branches from the right vagus and a few fibers from the left vagus nerves. Occasionally a small group of fibers may be seen on the adventitia of the portal vein.

The nerves were dissected free from the hepatic artery near its origin and sectioned. There was an immediate augmentation of bile flow from 10 to 70 per cent, averaging 36 per cent. A drop in general blood pressure usually followed this procedure, although it returned to a normal level after a few minutes. This confirms the observations made by Tanturi and Ivy¹⁴ and provides additional evidence that the hepatic nerves in some way regulate bile secretion.

TABLE IV
RESULTS OF EFFECT OF DISTENTION OF URINARY BLADDER ON BILE FLOW
BEFORE AND AFTER SECTION HEPATIC NERVES

Dog No	Distention of Bladder			Section Hepatic Nerves			Distention of Bladder After Section Hepatic Nerves		
	Control Bile Flow —Cc Per Hour	Dur-ing Disten-tion	Per Cent Change	Control —Cc Per Hour	After Sec-tion —Cc Per Hour	Per Cent Change	Control —Cc Per Hour	Dur-ing Stimu-lation	Per Cent Change
2	3 0	2 1	-30%						
5	6 0	3 6	-40%						
6	6 0	3 6	-40%						
11							6 0	6 0	0%
	Stimulation Nerve Erigens						Stimulation Nerve Erigens After Section Hepatic Nerves		
28	3 0	2 1	-30%	3 6	6 0	+40%	3 6	3 9	+9%
	5 4	3 0	-40%				4 2	4 2	0%
29	5 4	3 6	-33%	4 2	9 0	+54%	4 5	4 2	-7%
30	9 0	6 0	-33%	7 2	9 6	-33%	7 8	7 2	-8%
							9 6	9 0	-7%
31	5 4	3 0	-45%	7 2	8 4	+16%	6 6	6 0	-10%
	5 4	3 3	-39%				7 2		
							7 2	6 6	-8 9%

When the colon was redistended after section of the hepatic nerves in four dogs, there was little or no change in bile flow, the changes varied from 0 to -10 per cent, or averaged -0.8 per cent (Table I). The colonic nerve was restimulated three times in two dogs, no change occurred in two instances, and -12 per cent change occurred in the remaining dog (Table II). Stimulation of the inferior mesenteric plexus, a total of seven times in three dogs, was followed by alterations of +7 to -5 per cent from the control

flow, the average changes being ± 0.8 per cent (Table II). Five stimulations in two dogs resulted in no change when the superior mesenteric plexus was stimulated after section of the hepatic nerves, except a -9 per cent decrease on one occasion. Similar results are noted in Table IV when the bladder was redistended or the pelvic nerve restimulated after section of the hepatic nerves.

It is obvious from these results that the integrity of the hepatic nerves is essential for the observed inhibition of bile formation when the colon or bladder is distended or when the mesenteric nerves are stimulated. This proves the inhibition is due to a nervous reflex mechanism. The slight inhibition in flow after section of the hepatic nerves in a few cases suggests that some of the fibers may not have been divided.

In seven dogs whose blood pressure was below 60 Mm Hg, inhibition of bile flow did not take place when the colon was distended or its nerve supply stimulated, and in three of this group there was a slight increase in the rate of flow. The dog's general condition was either so poor that the normal reflex response could not be elicited or the resultant increase in blood pressure improved the circulation through the liver so as to augment its bile secretion.

Acholia, associated with a markedly congested liver, developed in one dog during the course of the experiment. The bile flow did not become reestablished after the intravenous administration of sodium dehydrocholate. The common duct was not kinked.

Observations during the experiments, as well as other work on acute biliary fistula animals, suggest that the concentration or viscosity of the bile varies inversely with the rate of flow. When the flow from the liver increased the concentration decreased, which would produce a thicker bile that might favor precipitation of its constituents and flow more slowly through the bile passages.

Discussion—The mechanism of this reflex response involves an analysis of the known effects of stimulation of the nerve supply to the liver, particularly in connection with bile formation. Stimulation of the hepatic or splanchnic nerves causes definite vasomotor changes in the liver. Bayliss and Starling,¹⁵ Francois-Franck and Hallion,¹⁶ Burton-Opitz,¹⁷ and Bauer, Dale, Poulson and Richards¹⁸ observed an increase in blood pressure in both the hepatic artery and the portal system on stimulation of these nerves. A decrease of liver volume signifying vasoconstriction within the liver accompanied this stimulation and occasionally persisted after the stimulus was interrupted. Burton-Opitz¹⁹ showed that there is a diminished blood flow through the liver, and concluded that the arterial and portal vasomotor mechanisms are separate and do not depend one upon the other. Olds and Stafford,²⁰ later, found by injection methods that the terminal branches of the hepatic artery and portal vein separately communicate with the hepatic sinusoids, thereby placing the above physiologic observation on an anatomic basis as well.

Lundberg²¹ and Hillyard²² sectioned the nerve supply to the liver in chronic biliary fistula dogs and reported no change in the output of bile. Tanturi and Ivy,¹⁴ in acute experiments, recently observed an augmentation of bile flow following section of the splanchnic or hepatic nerves and an inhibition when the distal ends of these nerves were stimulated, providing evidence that the rich nerve supply to the liver has some control over the secretion of bile.

The following possibilities may be offered to explain the inhibitory reflex effects on bile flow brought about by stimulation of the nerves mentioned above: (a) constriction of the intrahepatic biliary channels, thereby obstructing the flow of formed bile, (b) kinking of the bile canaliculi which form a diffuse network around the portal branches, (c) contraction of Glisson's capsule, (d) by constriction of the intrahepatic veins, thereby increasing the intrahepatic pressure to such a point that it would overcome the relatively low pressure (25 to 30 cm. bile) in the bile channels, (e) changes in the minute blood flow through the liver, and (f) the presence of inhibitory-secretory fibers in the splanchnic nerves to the liver.

Constriction or kinking of the interlobular bile ducts, as a result of splanchnic nerve stimulation, is unlikely because the period of inhibition should then be followed by a period of increased flow due to the release of temporarily obstructed bile. This does not occur. Contraction of Glisson's capsule could explain the observations on a pressure basis.

Heidenhain²³ and Muir²⁴ believed from their observations that changes in blood flow affect bile formation. The increase in blood flow through the portal system following a meal²⁵ or bile salt injection²⁶ is associated or followed by an increased flow of bile from the liver. The choleresis reported by the local or general application of heat²⁷ is associated with increased blood flow. The inhibition of bile flow on splanchnic stimulation is associated with an inhibition in blood flow through the liver. Tanturi and Ivy¹⁴ found that the increased blood flow is associated with increased bile flow as long as it does not increase the intrahepatic pressure.

The fibers of the vagi have been found to exert an excitatory or inhibitory secretory effect in dog and monkey.²⁸ It is likely that the splanchnic nerves contain inhibitory-secretory fibers. However, it would be difficult to prove the presence of such fibers in the hepatic nerves since they exert such a marked effect upon hepatic circulation. The augmentation of bile flow following section of the hepatic nerves is only indirect and equivocal evidence that inhibitory fibers are being sectioned even though this response often continues after the blood pressure has risen to its normal level.¹⁴

The inhibition of bile flow from the liver due to nervous impulses from the colon in the dog and monkey offers proof of reflex pathways from the bowel to the biliary system and suggests that a diminished amount of a thicker bile may be elaborated. If this stasis in bile flow were continued by repeated stimuli from the colon, precipitation of calculi might be favored, and difficulties in the flow of bile through the ducts might result. Obviously,

it would be of interest to determine whether the same mechanism could be shown to exist in man. There is no reason, however, to doubt the existence of the mechanism in man.

CONCLUSIONS

(1) Distention of the colon in the dog and monkey caused an inhibition in the flow of bile from the liver. This distention had no effect on the bile flow when choleresis had been established by the injection of sodium dehydrocholate.

(2) A similar response following stimulation of the central end of the colonic, inferior mesenteric, superior mesenteric nerves and pelvic nerve indicates that this inhibition is of reflex origin. Section of the hepatic nerves is followed by an increase in bile flow and prevents the above effects.

(3) The possibility of inhibitory-secretory fibers in the splanchnic or hepatic nerves and the effect of alterations in the blood flow caused by excitation of these nerves on bile formation are two factors which may explain, in part, the reflex inhibition of bile formation that occurs on the stimulation of the afferent mesenteric nerves.

REFERENCES

- ¹ Riegel, C., Ravdin, I. S., Johnston, C. G., and Morrison, P. J. The Composition of Gallbladder Bile and Calculi in Gallbladder Disease. *Surg., Gynec., and Obstet.*, **62**, 933, June, 1936.
- Phemister, D. B., Aronsohn, H. G., and Pepinsky, R. Variation in the Cholesterol, Bile Pigment and Calcium Salts Content of Gallstones Formed in the Gallbladder and Bile Ducts with a Degree of Associated Obstruction. *ANNALS OF SURGERY*, **109**, 161, February, 1939.
- ² Ivy, A. C. The Physiology of the Gallbladder. *Physiol. Rev.*, **14**, January, 1934.
- ³ Potter, M. G. Observations of the Gallbladder and Bile During Pregnancy. *J. A. M. A.*, **106**, 1070, March, 1936.
- ⁴ Gerdes, M. M., and Boyden, E. A. Rate of Emptying of Human Gallbladder in Pregnancy. *Surg., Gynec., and Obstet.*, **66**, 145, February, 1938.
- ⁵ Riegel, C., Ravdin, I. S., Morrison, P. J., and Potter, M. G. Gallbladder Bile in Pregnancy. *J. A. M. A.*, **105**, 1342, October 26, 1935.
- ⁶ Huggins, R. R., Harden, Boyd, and Grier, G. W. A Study of the Relationship of Pregnancy to Disease of the Gallbladder. *Surg., Gynec. and Obstet.*, **61**, 471, October, 1935.
- ⁷ Blalock, A. A. Clinical Study of Biliary Tract Disease. *J. A. M. A.*, **83**, 2057, December 27, 1924.
- ⁸ Kocour, E. J. Diverticulosis of the Colon. *Am. Jour. Surg.*, **37**, 433, September, 1937.
- ⁹ Good, C. A., and Kirklin, B. R. Influence of Extrabiliary Disease on the Functions of the Gallbladder. *Am. Jour. Roent. and Rad. Ther.*, **37**, 346, March, 1930.
- ¹⁰ Boyden, E. A., and Birch, C. L. The Reaction of the Gallbladder to Stimulation of the Gastro-Intestinal Tract. *Am. Jour. Physiol.*, **92**, 287, March, 1930.
- ¹¹ Wilkinson, S. A. Chronic Cholecystitis Versus Irritable Colon. *J. A. M. A.*, **109**, 1012, September 25, 1937.
- Moore, E. C. Chronic Cholecystitis with Reference to the Irritable Colon. *Western Jour. Surg., Obstet. and Gynec.*, **46**, 244, May, 1938.
- Twiss, J. R., and Greene, C. H. Dietary and Medical Management of Disease of the Gallbladder. *J. A. M. A.*, **101**, 1841, December 9, 1933.

- ¹² Lahey, F H, and Jordan, S M Management of Biliary Tract Disease Am Jour Surg, 11, 1, November, 1931
- ¹³ Kunath, C A The Stoneless Gallbladder J A M A, 109, 193, 1938
- ¹⁴ Tanturi, C A, and Ivy, A C A Study of the Effect of Vascular Changes in the Liver and the Excitation of Its Nerve Supply on the Formation of Bile Am Jour Physiol, 121, 61, 1938
- ¹⁵ Bayliss, W M, and Stirling, E H Observations on Venous Pressures and Their Relationship to Capillary Pressure Jour Physiol, 16, 159, 1894
- ¹⁶ Francois-Franck, C A, and Hallion, L Recherches expérimentales sur l'innervation vaso-constrictive du foie Ant de physiol nom et path, 5, 908, 1896
- ¹⁷ Burton-Opitz, Russel The Vascularity of the Liver—The Motor Reaction of the Portal Radicles of the Liver Quart Jour Exp Physiol, 7, 57, 1914
- ¹⁸ Bauer, W, Dale, H H, Paulson, L T, and Richards, D W Control of Circulation Through the Liver Jour Physiol, 74, 343, 1932
- ¹⁹ Burton-Opitz, Russel The Vascularity of the Liver The Influence of the Greater Splanchnic Nerves Upon the Venous Inflow Quart Jour Exp Physiol, 5, 189, 1912
- ²⁰ Olds, J M, and Stafford, E S On Manner of Anastomosis and Portal Circulations Johns Hopkins Hosp Bull, 47, 176, September, 1930
- ²¹ Lundberg, H Bile Flow and Bile Output After Denervation of the Liver Am Jour Physiol, 98, 602, November, 1931
- ²² Hillyard, L V Effect of Denervation of Liver on Secretion of Bile Am Jour Physiol, 98, 612, November, 1931
- ²³ Heidenham, R Hermann's Handbuch der Physiologie, 1, 266, 1883
- ²⁴ Murk, J Uber den Einfluss sensibler Reizung auf die Gallenausscheidung Pfluger's Arch, 8, 151, 1874
- ²⁵ Herrick, J F, Essex, H E, Mann, F C, and Baldes, E J The Effect of Digestion on Blood Flow in Certain Blood Vessels of the Dog Am Jour Physiol, 108, 621, 1934, The Effect of Digestion of Food on Blood Flow from the Liver of Dogs Am Jour Physiol, 108, 52, 1934
- ²⁶ Schwiegk, von H Untersuchungen uber die Leberdurchblutung und der Pfortaderkreislauf Arch f Exp Path u Pharm, 168, 693, 1932
- ²⁷ Osbourne, S L, and Goldman, L The Effects of Heat on Bile Flow, A Quantitative and Qualitative Study Proc Am Phys Soc, 179, April 26, 1939
- ²⁸ Tanturi, C A, and Ivy, A C On the Existence of Secretory Nerves in the Vagi and the Reflex Excitation and Inhibition of Bile Secretion Am Jour Physiol, 121, 270, January, 1938

CIRCULATORY PROBLEMS OF SURGICAL IMPORTANCE IN THE DIAGNOSIS OF ABDOMINAL LESIONS*

J STEWART RODMAN, M D , AND WILLIAM G LEAMAN, M D

PHILADELPHIA, PA

FROM THE DEPARTMENT OF SURGERY AND CARDIOLOGY, WOMAN'S MEDICAL COLLEGE OF PENNSYLVANIA, PHILADELPHIA, PA

Most of the papers presented before the American Surgical Association on the subject of cardiovascular disease naturally feature the results obtained from direct surgical attack in its relief. It seemed to us it might be worth while to discuss certain problems presenting difficulties in differential diagnosis and, therefore, in the proper management of various types of cardiovascular lesions which have confused surgeons from time to time in distinguishing them from the acute surgical abdomen. We cannot lay claim to originality in recognizing these difficulties. All of these problems have been met with before, but in isolated case reports, and so we hope that it might serve a useful purpose to group them into one working classification. Our object, therefore, in presenting this paper is to again stress these diagnostic pitfalls which we must avoid in distinguishing between the so-called acute surgical abdomen demanding immediate operative interference, and instances of cardiovascular disease *equally demanding* that operative intervention shall be withheld. It has proved to be most helpful to us in estimating the surgical risk to classify our cases with surgical lesions complicated by cardiovascular handicaps according to a grouping of such risks published by us in a previous paper.¹ Now, based upon the combined experiences of the Departments of Surgery and Cardiology at the Woman's Medical College Hospital, and more particularly upon that of the latter department, of the last eight years in the study of 4,083 cases, we wish to classify the types of cardiovascular disease giving rise to abdominal symptoms and to briefly cite cases illustrative of each type occurring in our services (Table I).

Mode of Production of Symptoms—Abdominal symptoms may be produced by almost any of the etiologic types of heart disease. The mechanism of the production of the symptoms, however, is variable. For example, the failure of the heart as a pump causing congestion of the abdominal organs is usually first reflected in enlargement of the liver. Rheumatic heart disease with mitral stenosis is to be suspected in over 50 per cent of these cases. However, hypertensive or arteriosclerotic heart disease may be the causative agent. Continued untreated congestive cardiac failure may produce symptoms usually encountered in gastro-intestinal tract disease—gas, anorexia, nausea, vomiting, diarrhea, fulness and pain in the abdomen, and loss of weight. Mild, yet clinically detectable, degrees of jaundice may be added to the symptom of right upper quadrant pain caused by sudden distention of

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13,

TABLE I

CLASSIFICATION OF CIRCULATORY DISTURBANCES OCCASIONALLY PRODUCING ACUTE
ABDOMINAL SYMPTOMS

- (1) Cardiac Failure
 - (A) Congestive Type
 - Liver Enlargement (right upper quadrant pain)
 - G-I Tract Congestion (nausea, vomiting, gas, hemorrhage, *etc*)
 - (B) Coronary Type (reflex)
 - Angina (pain referred to upper abdomen)
 - Coronary Occlusion (similar mechanism)
- (2) Pericarditis
 - (A) Acute Pericarditis (pain at times referred to abdomen)
 - (B) Calcific Pericarditis (cardiac compression Ascites may be an early symptom)
- (3) Embolism and Thrombosis
 - (A) Mitral Stenosis (auricular fibrillation) Emboli from large left auricle to splenic, renal, superior mesenteric and inferior mesenteric arteries
 - (B) Subacute Bacterial Endocarditis (infected emboli from the left side of the heart
Same locations as above)
- (4) Organic Vascular Change
 - (A) Aortic Aneurysm
 - (a) Symptoms produced by tumor growth
 - Displacement of organs
 - Vertebral erosion
 - (b) Symptoms produced by rupture or dissection
 - (B) Arteriosclerosis Spasm (abdominal angina)
 - Hemorrhage (in hypertension)
 - Thrombosis

the liver capsule, completing the masquerade ² Ascitic fluid in small amounts may arise to further complicate the picture

In certain types of heart disease, embolism is a frequent mode of production of confusing abdominal symptoms. Again, patients with mitral stenosis and enlargement of the left auricle constitute the majority of this group. Subacute bacterial endocarditis, with its tendency to involvement of the left side of the heart, is likewise a dangerous threat to the integrity of the arterial circulation below the diaphragm. Emboli in vessels supplying the abdominal organs may be responsible for the sudden onset of symptoms simulating a variety of surgical lesions. Occlusion of the mesenteric vessels presents a picture often diagnosed intestinal obstruction. A renal haven for the embolus simulates calculus while a splenic point of rest may give a sudden pain high up in the left quadrant of the abdomen simulating a ruptured viscus.

Referred pain from coronary artery disease with angina, or more frequently occlusion, may simulate any type of gastro-intestinal tract disturbance. The initial studies of Head³ and Mackenzie⁴ have, in recent years, been amplified in monographs by Capps⁵ and Jones⁶. The mechanism of pain of the referred type is too well known to need any particular comment here. The abdominal areas of expression in cases of angina and occlusion, and infrequently in cases of acute pericarditis, may simulate gallbladder disease, ulcer or acute pancreatitis. A reversed pathway may explain changes in the cardiac rhythm and even in the form of the electrocardiogram, although the

change arises from a gallbladder focus. Recent experiments upon dogs by Owen,⁷ and Crittenden and Ivy⁸ have served to prove that this mechanism is more than a mere possibility. Stimulation of the vagus nerve by disturbances in the gallbladder is no doubt the fundamental cause.

Palpable abdominal masses due to aneurysmal dilatations of the abdominal aorta, particularly when they occur in women, are puzzling to the surgeon. Rupture or dissection of the aneurysm produces an acute picture rarely correctly diagnosed and often leading to an unnecessary celiotomy. Smaller hemorrhages, although productive of the same degree of confusion, may occur in abdominal organs in hypertension. Arteriosclerosis of the abdominal vessels may lead to thrombosis, and the clinical picture will depend upon the size and location of the vessels involved. Reduction of the blood supply in

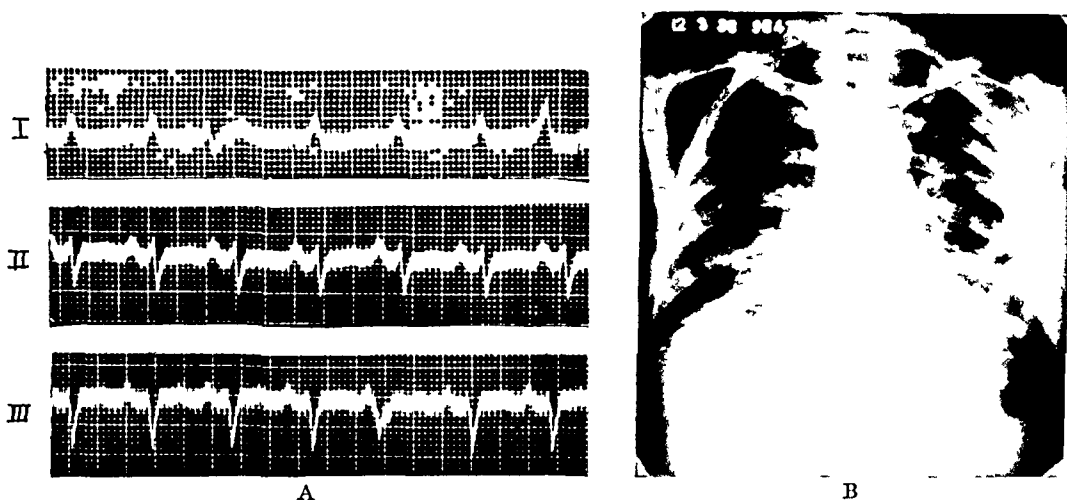


FIG 1—Case 1. (A) The electrocardiogram shows evidence of myocardial damage in QRS changes. (B) Roentgenogram shows cardiac enlargement of the hypertensive type.

the absence of thrombotic occlusion may give rise to abdominal symptoms that have been grouped under the clinical head of abdominal angina. Lack of proper blood supply (ischemia) when the demand on the gastro-intestinal tract is greatest (after meals) produces pain.

ILLUSTRATIVE CASES

Case 1—Right upper quadrant pain due to enlargement of the liver from cardiac failure simulating gallbladder disease.

Hosp No 2136. A. C., a physician, age 63, was admitted to the hospital, with chief complaint of right upper quadrant pain of two weeks' duration. Following a respiratory infection the patient experienced pain followed by anorexia, nausea, occasional vomiting and a slight tint of icterus. There was dyspnea present which he attributed to persisting cough.

Examination showed normal temperature, pulse 116, respiration 22, and blood pressure 122/80. The liver was large and tender. Rales were heard at the lung bases and the heart was enlarged to percussion 2 cm. to the left of the M.C.L. The heart sounds were distant and a soft apical systolic murmur was heard. The rhythm was regular. There was no edema. Roentgenologic examination of the chest (Fig 1) confirmed the presence of cardiac enlargement, and electrocardiographic study pointed also to the primary cardiac origin of the abdominal symptoms. Blood count, Wassermann and urine were negative. The icterus index was 18.

Discussion—Cases of this type are not at all uncommon. It is interesting to note that this patient was a physician who interpreted the symptoms of right upper quadrant pain, nausea, vomiting and slight icterus entirely in the light of gallbladder disease and requested admission to a surgical service. The upper respiratory tract infection no doubt was the immediate cause of the upset, and the patient explained his dyspnea and cough entirely on this basis. The rapid onset of the right-sided cardiac failure caused marked engorgement of the liver with stretching of the capsule, this focused attention on the gallbladder as a primary source of the trouble due to the localized pain and tenderness. The other gastro-intestinal symptoms were produced by stasis of blood in the areas drained by the portal circulation. Even hemorrhage at times can occur in these cases with long-standing congestion due to ulceration in the devitalized areas of mucosa.

Symptoms of this type in patients in the younger age groups are generally due to advanced mitral stenosis and are then less apt to be confused with the symptoms of gallbladder disease.

Bed rest and rapid digitalization in this case promptly resulted in improvement in the gastro-intestinal symptoms. The liver diminished in size and the tenderness disappeared. Some weeks later the patient began to experience attacks of paroxysmal cardiac dyspnea (cardiac asthma), nocturnal in type, giving further evidence of the true nature of the underlying process.

An interesting fact in this case was the complicating jaundice. Rarely can this symptom occur in such a marked degree in the absence of true disease of the digestive apparatus. Retention of bilirubin here was sufficient to impart a distinct tint to the skin and sclerae. The congestive failure impaired the excretory function of the liver, since an organ suffering from the effects of so marked an anoxemia is unable to excrete a larger amount of bile pigment. The nutmeg liver, the term applied to the organ in this condition, shows on microscopic section compression of the central cells of the liver lobule.

At times, especially in mitral stenosis, jaundice may suddenly appear following a pulmonary infarction. Although this was first believed to be caused by the extra load of hemoglobin capable of breaking down and producing excess bilirubin, it has since been shown to be due to the intensification of the anoxemia of the liver cells following the infarction.

The investigations of Rich and Resnick¹¹ support this view. Kugel and Lichtman,¹⁰ more recently, in an analysis of clinical and pathologic material, studied all aspects of the subject and advanced the following explanation for the frank jaundice seen in cardiac failure of the type described in Case 1.

"In a patient with a long standing pulmonary stasis due to cardiac insufficiency, pulmonary infarction occurs. From this rich source, hemoglobin is made available by destruction and hemolysis of red blood cells and bilirubin is rapidly formed. The presence of serum in the lung, owing to the congestion and often to infection, facilitates the solution and absorption of the bilirubin. The capacity of the liver to excrete the substance is impaired owing to the anoxemia and to the toxic effect of infection on the parenchyma of the liver.

However, unless extensive disease of the liver, i.e., true cirrhosis, is present, the causation of the frank jaundice is primarily pulmogenic. The deleterious effects of anoxemia and of infection on liver cells play a necessary but only a secondary rôle. The pulmonic factors of primary importance are the duration and type of the heart failure, i.e., prolonged failure of or obstruction in the left side of the heart and pulmonary congestion and the local factors favoring the rapid formation and absorption of bilirubin, i.e., pulmonary infarction, hemolysis of erythrocytes and local or systemic infection."

Case 2—Abdominal pain and liver enlargement followed by ascites due to calcific pericarditis causing cardiac compression

Hosp No 1325 R F, age 12, was admitted to the hospital, complaining of abdominal pain and tenderness and increase in abdominal size of three years' duration. There was dyspnea and, lately, pretibial edema. The past history was negative for rheumatic infection. Examination showed a blood pressure of 90/60, a systolic apical murmur and little or no increase in cardiac size. There was noted distention of the jugular veins (venous pressure 240 Mm). Marked ascites was present. Fluoroscopy showed a small, quiet heart and oblique roentgenogram of the heart demonstrated the presence of an encasing shell of calcium.

Discussion—In this patient, deposits of calcium about the heart caused compression and faulty diastolic filling, these were responsible for the presenting abdominal symptoms. The diagnosis was suspected when studies revealed a small, quiet heart, a rising venous pressure, and a falling systemic pressure. Attention was directed away from the abdomen, and thoracic surgery was advised to relieve the symptoms of cardiac compression.

Acute pericardial processes, particularly in children, may be accompanied by pain referred to the abdomen. In some cases acute inflammation of the appendix may be suspected and operation performed. Pain in acute pericarditis usually results from extension of the inflammatory process to the mediastinum or to the diaphragmatic pleura. This type of pain may give abdominal reference but careful study of the heart should reveal the true underlying cause. Detection of the characteristic pericardial friction rub many times serves to clear the diagnosis. When the process extends to the diaphragm, cough and deep breathing accentuate the pain and this is important in the differential diagnosis. The pericarditis met in terminal conditions like nephritis never gives pain referred to any abdominal area due to the absence of the complicating pleuropericarditis. In one patient in our series, abdominal pain was found to be caused by acute rheumatic pericarditis. A second attack a few weeks later, accompanied by rectus rigidity, was proved to be due to rheumatic involvement of the appendix, the appendix on section showing typical Aschoff bodies.

Case 3—Coronary sclerosis followed by acute coronary occlusion, diagnosed gall-bladder disease

Hosp No 763 N M, male, age 51. When first seen this patient complained of indigestion and gas and occasional pain over the right upper abdomen. Dyspnea and palpitation had been experienced for some years. No edema or chest pain. The significant findings were overweight, slight increase in blood pressure (163/92), occasional pre-

mature beats, but not much increase in heart size. The electrocardiogram (Fig 2 A) showed only a left axis deviation. The patient was placed on a dietary regimen and told to make arrangements for a gallbladder roentgenologic study. This he failed to do, and when next seen, four months later, he showed no improvement. The indigestion was worse, the dyspnea was increasing, and he stated that a week before the second examination he had experienced a very severe attack of indigestion. This attack came on at night, awakened him from his sleep, and required a hypodermic injection of morphine for relief. Another electrocardiogram (Fig 2 B) showed the presence of a recent coronary occlusion of the posterior type.

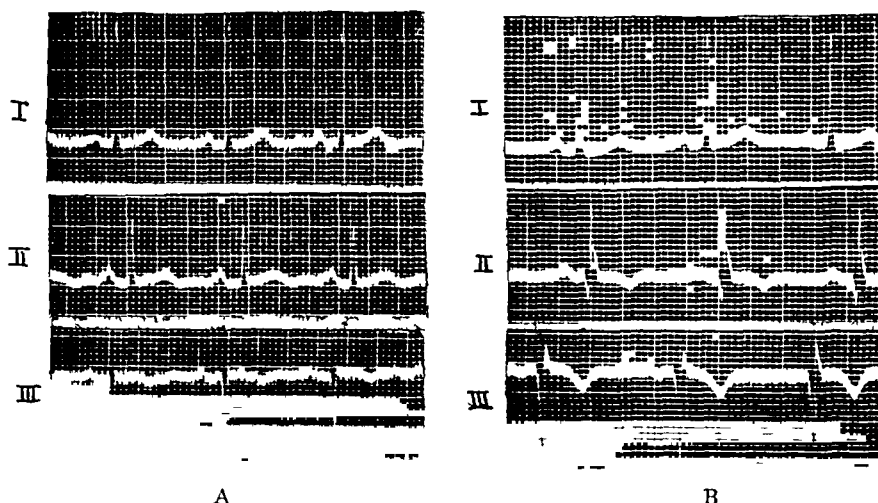


FIG 2 —(A) Electrocardiogram on first examination shows only a left axis deviation. (B) Second tracing showing presence of coronary occlusion of posterior type.

Discussion—Differential diagnosis in this type of patient is usually more difficult. Many times, in patients of this age and build, it is not infrequently discovered that gallbladder disease and coronary disease coexist. This has led to a great deal of discussion and much speculation in the literature. The exact relationship between a diseased gallbladder and the heart remains a complex subject although convincing electrocardiographic evidence of improvement has at times been observed to follow cholecystectomy.¹³ Many investigators have also demonstrated the existence of important reflex pathways between the gallbladder and the heart. Even effects upon the cardiac rate and rhythm have been shown to occur at the time of operation. It has been our impression in a number of these cases, where striking postoperative improvement in the pain has been observed, that our initial opinion as to the degree of coronary involvement was incorrect. In other words, most of the symptoms were produced by disease in a high lying gallbladder.

Our chief concern, therefore, lies in the correct identification of the major lesion. The pain of acute coronary occlusion is often confused with the pain produced by gallstones and a celiotomy performed.^{14, 15, 16} Pain, vomiting, fever, and leukocytosis are commonly met with in both conditions. However, if the past history is carefully reviewed, the patient with gallbladder disease will usually be found to have a history of indigestion, while the patient with coronary occlusion may give a history of mild attacks of angina resulting from effort. A complete cardiac study, using the form suggested by us,¹ will

seldom fail to throw considerable light on the correct diagnosis. In Case 3, the second electrocardiogram furnished the diagnosis and localized the infarction (Fig 2 B). The characteristic T-wave changes were seen. The degree of shock observed in coronary occlusion is not present in gallbladder disease nor is the sharp drop in the blood pressure so constant in gallbladder colic as it is in coronary occlusion. The appearance of a friction rub over the precordium in cases of anterior coronary occlusion clinches the diagnosis in favor of occlusion while the appearance of jaundice swings the balance toward gallbladder disease.

Cholelithiasis may cause, reflexly through the autonomic nervous system, certain changes in the rhythm of the heart.¹⁷ Babcock¹⁸ believes that inhibition of the heart can be caused by stimulation of the filaments of the vagus

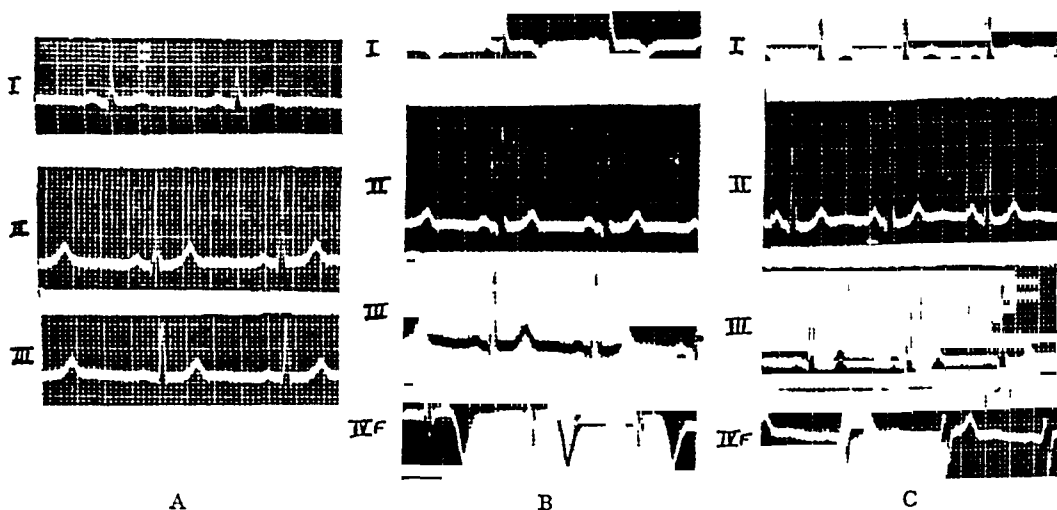


FIG 3—(A) Electrocardiogram on admission shows little change. (B) Taken eight hours after A. Note change in T₁ and T₄ indicative of anterior coronary occlusion. (C) Showing return of the electrocardiogram to normal eight months later.

arising from the wall of the gallbladder. Heart block, relieved by atropine, has been reported to result from gallbladder stimulation. The jaundice produced in some patients by gallbladder disease may secondarily affect the cardiac mechanism. Systolic apical murmurs have been reported, by some observers, appearing during pain from a gallbladder focus. Consequently the only reliable electrocardiographic evidence in the differential diagnosis lies in the T-wave alterations seen in the patient we have presented.

Case 4—Coronary sclerosis followed by acute coronary occlusion diagnosed ruptured peptic ulcer.

Hosp No 4027 J M, male, age 50, was admitted to the College Hospital, July 6, 1938, with chief complaint of sudden, severe epigastric pain coming on while at work. He gave a history of two years' treatment for gastric ulcer. No roentgenologic study, however, had been made. When first seen, the patient was pale, sweating. Pulse 100, temperature 97° F, respiration 30. The heart was not enlarged, blood pressure 100/70. There was upper abdominal tenderness, but no marked rigidity. WBC 12,000. The first electrocardiogram was negative. The pain was completely relieved following injection of ¼ gr of morphine. A second electrocardiogram taken a few hours later showed marked change (Figs 3 A and B).

Discussion—The previous history of digestive disturbance complained of by this patient was no doubt caused by his cardiac lesion. He presented this vague type of "indigestion" for some years. Although he was never fully studied to prove the diagnosis of peptic ulcer before he was seen by us, it was assumed that the lesion was present due to the favorable effect of alkali therapy in improving the indigestion and "gas." The history of this type of treatment centered the attention at the time of the attack on the gastro-intestinal tract, and the erroneous diagnosis of ruptured peptic ulcer was made in the receiving ward and the patient placed on a surgical service. It is a matter of additional interest that the usual leads of the first electrocardiogram were entirely negative. As in many times the case, the typical electrocardiographic changes did not develop entirely until 18 hours after the onset of the attack. The second tracing shows characteristic changes in leads 1 and 4. At the same time a friction rub was heard over the precordium, clinching the diagnosis. It appears, then, that the dangerous period for the patient is the silent interval between the onset of the attack and the development of pathognomonic electrocardiographic and physical signs. This patient made a prompt and uneventful recovery. On March 11, 1939 (Fig 3C,) evidence of the accident had disappeared from all leads of the electrocardiogram. Subsequent roentgenologic studies failed to reveal an ulcer.

Case 5—Abdominal aortic aneurysm of arteriosclerotic origin simulating acute surgical abdomen at time of dissection prior to final rupture.

Hosp No 3784 F E, male, age 68, had been healthy, except for occasional attacks of indigestion, until the sudden onset of a tearing pain in the upper abdomen with radiation to the right lumbar region. It was accompanied by sweating, pallor and vomiting, and when the patient attempted to go to the bathroom, the slight exertion caused him to fall to the floor in collapse. There was involuntary emptying of the bladder and bowel. When first seen, he was pulseless with rapid shallow respirations. The picture was one of impending dissolution. The abdomen showed a board-like rigidity and the temperature by rectum was 95° F. In 20 minutes, the patient regained consciousness and the pulse became perceptible at the wrist. He complained of pain in the upper abdomen and vomited again. A diagnosis of perforated peptic ulcer was made and operation advised. Further observations changed this diagnosis when the patient quickly improved and the board-like rigidity of the abdomen disappeared. A mass, thought to be an aneurysmal sac, was palpated and on account of continued abdominal pain, the patient was given large doses of morphine and placed on shock treatment. The patient showed rapid improvement in blood pressure, color and pulse volume for 36 hours. At the end of that time there was a recurrence of severe abdominal pain, again accompanied by signs and symptoms of profound shock. Board-like abdominal rigidity did not recur and the aneurysmal sac was distinctly felt. It was more tender and larger in size and there was a bulging in the right flank. The patient showed marked pallor, and gave no response to the usual measures. He died in coma in two hours.

Autopsy showed no peptic ulcer, but advanced atherosclerosis of the aorta, an abdominal aortic aneurysm with rupture. The entire right side of the abdomen from the spinal column to the lateral wall and from the liver to the pelvis was filled with massive retroperitoneal blood clot that had pushed the posterior peritoneum so far forward that it was nearly in contact with that of the abdominal wall (Fig 4). The hemorrhage had

pushed into and split the mesentery of the cecum and ascending colon. The mesentery of the small bowel was not affected. The kidney, ureter, adrenal gland and other retroperitoneal structures floated in the enormous clot.

Retroperitoneal Space and Structures—Aorta. The wall was thin and inelastic, and the intima was pitted and cracked with atheromatous ulcers. Just distal to the origin of the superior mesenteric artery, extending to and involving the bifurcation, was a large, fusiform dilatation which projected forward and to the left into the abdomen. After removal this measured 14×8×6 cm. The root of the mesentery lay across its anterior sur-



FIG. 4—Drawing showing relationship of aneurysmal dilatation to surrounding structures. (Reprinted from New International Clinics, 1, Series 2, through courtesy of J. B. Lippincott Co.)

face. When opened, the forward bulging portion was found to be filled by layers of dense yellow fibrin. The wall was continuous with that of the aorta, overlaid and reinforced by peritoneum and its connective tissue, to which it was closely adherent. The lumen of the vessel, which went through the mass against the posterior wall, was lined by a smooth, red layer of fresh thrombus. In the central portion of this thrombus was a small fissure which overlaid a short (1 cm.) irregular rupture in the posterior wall of the vessel.

Discussion.—Abdominal aortic aneurysm is a rare although extremely important lesion to keep in mind in connection with circulatory problems that figure in the differential diagnosis of abdominal lesions. Symptoms from its

rupture or dissection often confuse the surgeon in the diagnosis of abdominal emergencies, puzzle the urologist, when small hemorrhages invade the tissues about the kidney or press on the ureter, and frequently tax the diagnostic acumen of both internist and neurologist in interpreting pain referred to various sections of the body.

It is surprising how large abdominal aneurysms may become and how great a displacement of the abdominal organs they may cause and still elude clinical detection if the sac points posteriorly and does not erode the vertebrae. Thompson¹⁹ reported an abdominal aneurysm, in a laborer, age 39, which contained six and one-half quarts of fluid blood and clots at autopsy. This aneurysm had pushed both kidneys so far forward that they were diagnosed as metastatic masses on palpation. This patient had not consulted a physician until the last few weeks of life. Many cases reported in the literature were not seen until they had become moribund following perforation or dissection. When subjective symptoms from these cases are tabulated, the most frequently recorded is pain. It may be of any variety from a vague type of abdominal discomfort, occurring at times in patients before rupture, to the typical, agonizing terminal variety of pain attending the tearing of the aortic wall. The type of pain experienced by the patient in these vascular accidents is outstanding. Extremely large doses of morphine seem ineffective in such calamities and these circumstances alone should always suggest an abdominal vascular complication. The ensuing symptoms of profound shock add further evidence. Many times, in the cases reported in the literature and in our case, preliminary smaller ruptures precede the final event. The intermittent hemorrhages confuse the picture and often unnecessary surgical exploration is undertaken. The distribution and character of the pain at the time of rupture depend on the location of the aneurysm and the point of rupture. Extravasations into the retroperitoneal space (Case 5) are frequent. If either kidney or the ureter is involved, renal colic is simulated and the pain may radiate down the inner aspect of the thigh to the testicle. The high site of the rupture, as in this case, often leads to the diagnosis of ruptured peptic ulcer.^{22, 23} This was the impression of the first physician to reach the patient's side. Vomiting and diarrhea are frequently present and serve to further complicate the picture.

Figure 5, compiled from cases reported in the literature, shows the variety of symptoms that may result from rupture, pressure or dissection when various structures of the body are involved.²⁴ (1) Retroperitoneal rupture with perinephric collection simulating abscess,^{25, 26, 27} (2) pressure on ureter with picture of uremia,²⁸ (3) rupture into the gastro-intestinal tract (duodenum^{29, 30, 31, 32})—pressure on duodenum gives symptoms of pyloric obstruction,³³ (4) rupture into the peritoneal cavity,³⁴ (5) rupture simulating psoas abscess,³⁵ (6) dissection with pressure on iliac arteries followed by gangrene,^{36, 37} (7) rupture through the diaphragm into the pleural cavity with symptoms of thoracic disease,³⁸ (8) spinal erosion with pain in the back and legs,³⁹ and (9) rupture into the inferior vena cava (arteriovenous aneurysm). Consequently, abdominal aneurysms may produce melena, hemoptysis or

hematemesis Portal, splenic or mesenteric vein thrombosis may occur and give the first clue to the presence of an aneurysm^{40, 41}

The clinical diagnosis of abdominal aortic aneurysm rests upon the demonstration of a pulsating, expansile tumor mass⁴² This sign was present at the time of the second examination of Case 5 Inspection in this case showed a very slight anterior bulge of the abdominal wall but no pulsations could be seen At times a thrill may be palpable over the suspected mass Palpation, carefully carried out, usually clinches the diagnosis The tumor mass, when

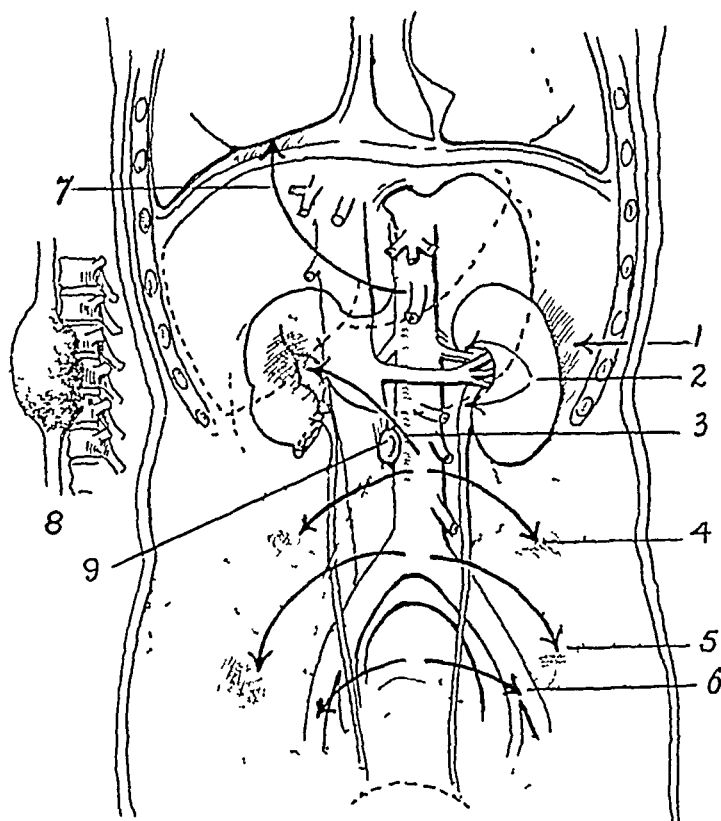


FIG 5—Diagram showing organs involved and pathways of dissection in reported cases of ruptured abdominal aortic aneurysms (Reprinted from New International Clinics, 1 Series 2, by permission of the J B Lippincott Co)

grasped, shows expansile pulsation as well as upward thrust It will seldom be found to move with respirations If the aneurysm is high up under the diaphragm, or if it points posteriorly, palpation of the sac may be difficult or impossible Often, on auscultation, a systolic murmur is heard over the mass In some instances, the patient presents himself with the chief complaint of pulsating abdominal tumor mass (described by one patient as an "extra heart") The pulsating aneurysmal sac must be differentiated from the throbbing abdominal aorta and from tumor masses overlying and transmitting pulsations of the aorta In patients where the thickness of the abdominal fat is not too great and the musculature not too rigid, differentiation of an aortic aneurysm from a visceral tumor mass may readily be made if the patient assumes the

knee-chest position The tumor will fall away from the aorta and no longer transmit the pulsation to the examining hand

It is well to remember in cases of suspected abdominal aortic aneurysm that a marked pulsation of the aorta is met in cases of extreme anemia, in patients with aortic insufficiency, in hyperthyroidism and in many underweight, neurotic individuals In these cases it may be possible to grasp the vessel in the hand and the diagnosis of aneurysm is often made More detailed examination will always show that only an up and down throbbing is present and no lateral expansile pulsation However, if the aneurysm is completely filled with clotted blood, it may closely simulate a tumor mass and in these cases roentgenologic examination proves invaluable^{43, 44, 45, 46} Many times roentgenograms will reveal a pressure erosion in the vertebral column⁴⁷ and avoid an unnecessary laminectomy This erosion is searched for between the eleventh dorsal and third lumbar segments The most frequent combination is the erosion of the twelfth dorsal and first lumbar segments⁴⁸

We have encountered abdominal aneurysms three times, proving the diagnosis in each instance, in 4,058 patients referred to the Cardiac Clinic of the Women's College Hospital during the past eight years All were encountered in men past 60 years of age, and all were of the atherosclerotic type

Another case showing rupture of the aorta with severe abdominal pain and presence of a palpable mass was recently seen by one of us at the Bryn Mawr Hospital

Case 6—Rupture of the thoracic aorta with dissection, diagnosed gastro-intestinal tract malignancy and perforation

H T, colored, female, age 41, was admitted to the hospital, complaining of a sudden, severe, agonizing abdominal pain Vomiting occurred soon after the onset which was later bloody and was attended by collapse Examination showed a markedly enlarged heart mostly in the region of the left ventricle, no murmurs, normal rhythm The abdomen was distended with a nonpulsating, tender, rounded mass in the right upper abdominal quadrant, extending to the right lower quadrant, and about the size of a large grapefruit Other abdominal areas were quite tender Peristalsis could be made out in the left upper quadrant but was absent elsewhere An electrocardiogram showed diphasic T-waves in Leads 1 and 2 and a left axis deviation Two days later there was recurrence of severe, sudden abdominal pain The patient quickly developed signs of profound shock and died in 20 minutes

Autopsy—Body of a colored woman, approximate age 41, quite obese There was a large area of ecchymosis in the right flank below the costal margin There was a low midline abdominal scar On removing the skin, the subcutaneous tissue of the right parietal abdominal wall was diffusely hemorrhagic There was a subserosal hematoma in the same area On opening the chest, the right pleural cavity contained a great quantity of serous fluid together with a huge blood clot The left pleural cavity contained a lesser amount of fluid and clot The pleural surface of the diaphragm on the right side appeared ecchymotic There was a diffuse hematoma beneath both right and left parietal pleurae as it joined the visceral pleura at the hilum

The heart, lungs, and aorta, down to the bifurcation of the common iliacs, were dissected *in toto* There was noted diffuse hemorrhagic spreading from the posterior mediastinum downward along the aorta retroperitoneally On opening the aorta, it appeared atheromatous There was no intimal puckering There was what appeared to be a small perforation in the upper thoracic aorta with retropleural and retroperitoneal

hemorrhage The lungs were not adherent and gave no evidence of pathology (right lung 300 Gm, left lung 250 Gm)

Heart—Pericardium normal Myocardium hypertrophied and dilated, soft consistency Valves intact, no separation between the aortic leaflets (430 Gm)

Liver—1,300 Gm Appeared normal, gave evidence of passive congestion on section, no other gross pathology Gallbladder wall was slightly thickened and the gallbladder contained a solitary gallstone

Kidneys—Right 150 Gm Left 175 Gm Showed some slight decrease in cortical substance in proportion to the medulla There was a slightly generalized fibrosis There were small retention cysts in the upper pole of both kidneys

Spleen—100 Gm Normal size, grayish light pink in color, extremely soft

G-I Tract—Appeared normal with the exception of the sigmoid colon where there were numerous diverticula

Uterus was present and appeared atrophic

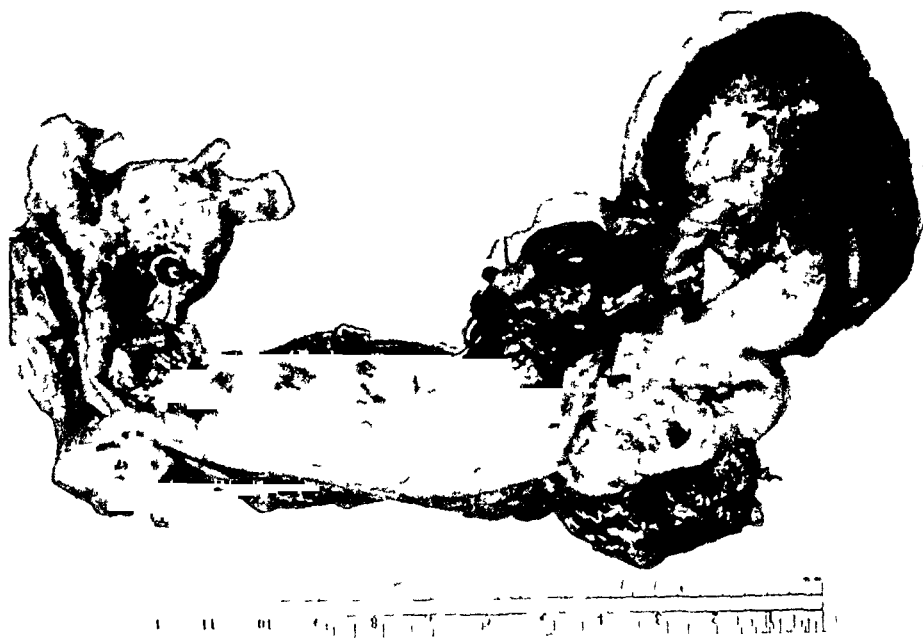


FIG 6—Autopsy specimen showing ruptured aorta and pathway formed by dissection

Cause of Death—Generalized atheromatosis with perforation of the aorta, hemothorax and retroperitoneal dissection

Note—After fixation in formalin, the heart and aorta were carefully dissected out The perforation appeared to be about 5 cm below the arch of the aorta in the posterior surface in correspondence with a deep-seated atheromatous ulceration From this point the blood appeared to have dissected out the adventitia for a short track, then breaking the adventitia and infiltrating the loose prevertebral tissue in the manner already described (Fig 6)

Case 7—Thrombosis of the superior mesenteric artery, diagnosed ruptured peptic ulcer

Hosp No 2263 R A, male, age 44 Well until six hours before admission, when he was awakened from sleep with severe pain in the right lower quadrant The patient described the pain as a "severe blow" Vomiting occurred several times and this was followed by diarrhea There were seven bowel movements between 2 A M and time of admission to the hospital at 7 A M The pain continued, increasing in severity and radiating to the back On admission, the patient appeared acutely ill There was dyspnea and

SYMPTOMATOLOGY OF VASCULAR PATHOLOGY

extreme restlessness from continuous pain The abdomen was distended with a board-like rigidity Tenderness was generalized There was no peristalsis and no masses were palpable A plain film showed stepladder formation of intestinal obstruction The pre-operative diagnosis was ruptured peptic ulcer At operation, thrombosis of the superior mesentery artery was found with intestinal obstruction and gangrene of the ileum (Fig 7) A cecostomy was performed, but the patient died two hours later

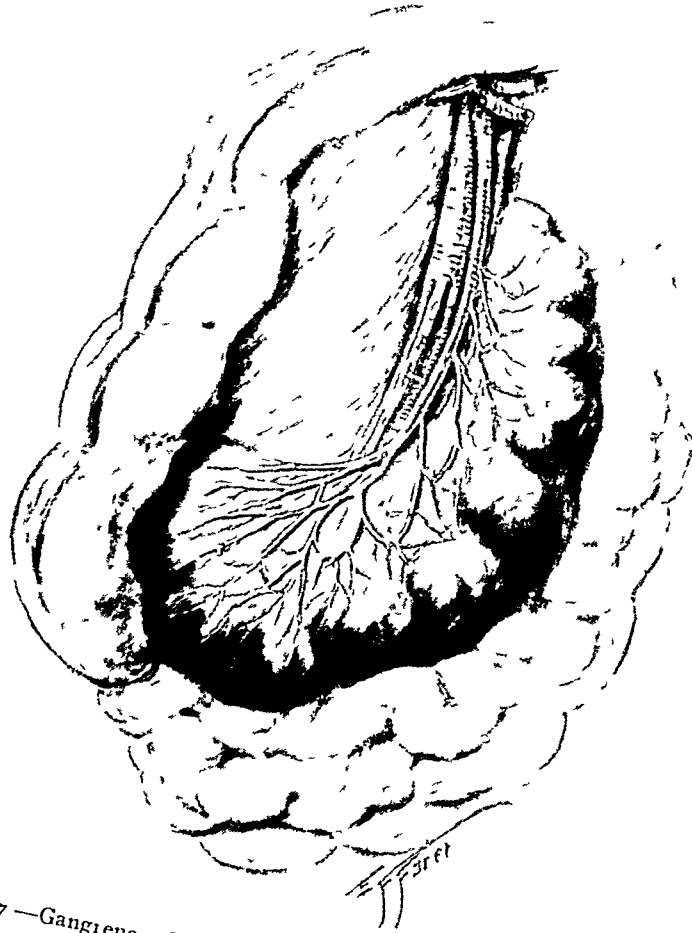


FIG 7—Gangrene of intestinal loop following thrombosis of superior mesenteric artery

Discussion—Embolism or thrombosis of the superior and inferior mesenteric arteries commonly occurs in the presence of endocarditis or arteriosclerosis Infarction almost always follows and the outcome, particularly when the superior mesenteric artery is involved, is nearly always fatal An embolus may arise from vegetations in the left side of the heart in cases of bacterial endocarditis, from a thrombus in the auricular appendix in advanced mitral disease with stenosis, and then it may lodge in one of the large branches of the superior mesenteric artery and almost always produces a fatal abdominal picture Atheromatous degeneration of the arterial wall may lead to the same catastrophe Rarely, thrombosis of the vein, secondary to acute appendicitis or an inflammatory process in the pelvis, may have the same effect The resulting infarct, nearly always of the red or hemorrhagic type, usually involves the

lower part of the ileum or jejunum, and this area quickly becomes gangrenous, resulting in a general peritonitis

As in the case described here, the onset of this condition is usually sudden, with acute, paroxysmal abdominal pain due to the cutting off of the blood supply to the segment of the bowel. Diarrhea is not uncommon. At times, the passage of blood by bowel suggests intussusception. Later, all the signs of obstruction appear with symptoms generally indistinguishable from those caused by internal strangulation. Accurate diagnosis, prior to operation, is

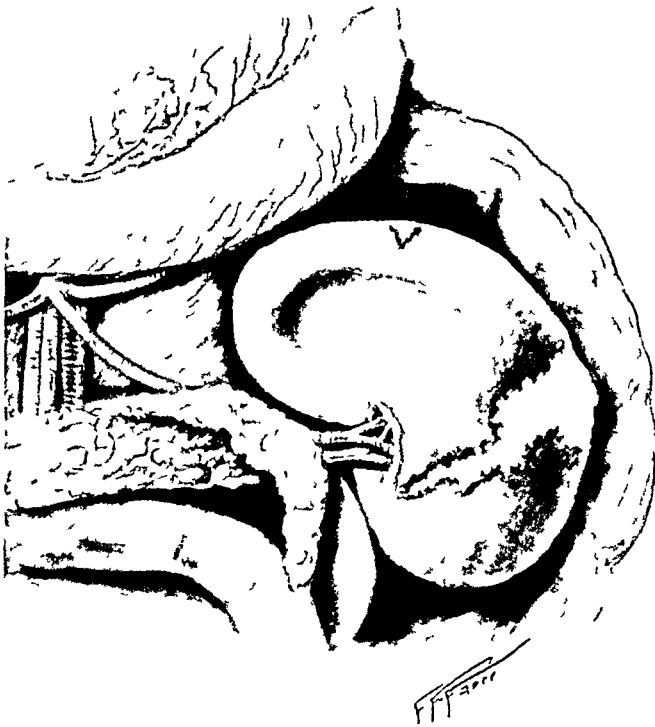


FIG 8—Infarct of spleen following embolism in case of subacute bacterial endocarditis

seldom made in these cases. They are usually diagnosed as acute intestinal obstruction or ruptured peptic ulcer.

Case 8—Subacute bacterial endocarditis, with splenic infarction, causing left upper quadrant pain

Hosp No 3279 R F K, male, age 31, was admitted to the Woman's College Hospital, complaining of pain and tenderness in the left upper abdominal quadrant, sudden in onset. Over the course of the previous two months, there had been progressive weakness, pallor and evening temperature of 100° F. He had been able to work until a week before admission. The past medical history was positive for rheumatic infection at age of 13. Examination showed temperature 101° F, pulse 110, blood pressure 150/40. There

was stenosis and regurgitation at both mitral and aortic valves. The spleen was palpable and tender. The fingers showed clubbing. A blood culture showed 125 colonies of *Streptococcus viridans* per cubic centimeter. Three weeks later, the patient sat up in bed and died suddenly with all symptoms of cerebral embolism. An autopsy confirmed the diagnosis of cardiac enlargement, aortic and mitral stenosis with superimposed vegetations of subacute bacterial endocarditis. The cause of the attack of acute left upper quadrant pain on admission is suggested by the splenic infarct shown in Figure 8.

Discussion—Subacute bacterial endocarditis is of surgical interest on account of the frequency in this condition of emboli to the abdominal organs with the production of symptoms simulating acute emergencies.⁵⁰ The splenic, renal and mesenteric arteries are, perhaps, in the order named, the most common sites for emboli to lodge. In the spleen, the infarct is of the anemic type, often multiple and ranging in size from that of a small pea to an embolus as large as the whole organ. The symptoms vary from none at all to a sudden sharp left upper quadrant pain of the type that brought this patient to the hospital for relief. Rigidity of the muscles over the area is not uncommon, and the pain is usually accentuated by breathing. Wedd⁴⁹ reports three cases of infarcted spleen following subacute bacterial endocarditis where celiotomies were performed for a ruptured abdominal viscus. Infection of the area of the infarct by bacteria in the embolus may occur with spread to the peritoneum, and death.

SUMMARY

The mode of production of abdominal symptoms by the following types of circulatory disorders is reviewed: Congestive cardiac failure with liver enlargement, chronic cardiac compression resulting from calcific pericarditis with enlargement of the liver and ascites, coronary occlusion and angina, abdominal angina, abdominal aortic aneurysm with rupture, rupture of the aorta with dissection, thrombosis of the superior mesenteric artery and embolism. Following the résumé of the record of each typical case, the diagnostic points essential in the detection of the cardiovascular background are discussed.

REFERENCES

- ¹ Rodman, J. S., and Leaman, W. G. The Surgical Risk with Special Reference to the Cardiovascular System. *ANNALS OF SURGERY*, 103, 13-23, January, 1936.
- ² Riesman, David. Myocardial Disease and Its Gastric Masquerades. *JAMA*, 91, 1521, 1928.
- ³ Head, H. On Disturbances of Sensation with Reference to the Pain of Visceral Disease. *Bram*, 16, 1, 1893.
- ⁴ Mackenzie, J. Symptoms and Their Interpretations. Shaw and Sons, London, 1912.
- ⁵ Capps, J. A. A. Clinical Study of Pain. Macmillan and Co., New York, 1932.
- ⁶ Jones, C. M. Digestive Tract Pain. Macmillan Company, New York, 1938.
- ⁷ Owen, S. E. A Study of the Viscerocardiac Reflexes. *Am Heart Jour*, 8, 496-506, April, 1933.
- ⁸ Crittenden, P. I., and Ivy, C. A Study of the Viscerocardiac Reflexes, II. *Am Heart Jour*, 8, 507-518, April, 1933.
- ⁹ Jump, H. D., and Leaman, W. G. The Abdominal Aortic Aneurysm. *New Internat Clinics*, 1, New Series, No. 2, March, 1939.
- ¹⁰ Kugel, M. A., and Lichtman, S. S. Factors Causing Clinical Jaundice in Heart Disease. *Arch. Int. Med*, 52, 1, 16, July, 1933.

- ¹¹ Rich, A R, and Resnick, W H On the Mechanism of the Jaundice Following Pulmonary Infarction in Patients with Heart Failure Bull Johns Hopkins Hosp, 47, 75, 1926
- ¹² Bettman, R B, and Rubinfeld, S H Gallbladder Reflexes in Man under Spinal Anesthesia Am Heart Jour, 10, 4, 550, April, 1935
- ¹³ Fitzhugh, T, and Wolferth, C C Cardiac Improvement Following Gallbladder Surgery ANNALS OF SURGERY, 101, 478, 1935
- ¹⁴ Willis, F A, and Fitzpatrick, J M Relationship of Chronic Infection of Gallbladder to Disease of the Cardiovascular System Iowa State Med Soc, 15, 589, November, 1925
- ¹⁵ Schwartz, M, and Herman, A The Association of Cholecystitis with Cardiac Infections Ann Int Med, 4, 783, January, 1931
- ¹⁶ Barker, P S, *et al* Abdominal Disease Simulating Coronary Occlusion Am Jour Med Sci, 188, 219, August, 1934
- ¹⁷ Percy, J F, and Howard, H Studies on the Visceral Nervous System Am Heart Jour 2, 530, June, 1927
- ¹⁸ Babcock, R H Ann Clin Med, 2, 203, 1922, J A M A, 73, 1929, 1919
- ¹⁹ Thompson, W G A Phenomenal Aortic Aneurysm Med Rec, 73, 636, 1908
- ²⁰ Cabot, Case 22151 Dissecting Aneurysm of the Thoracic and Abdominal Aorta with Partial Diagnosis of Dissection of the Left Renal and Left Common Iliac Arteries New England Jour Med, 214, 733-736, 1936
- ²¹ Cabot, Case 21011 Ruptured Dissecting Aneurysm of Abdominal Aorta New England Jour Med, 212, 26-28, 1935
- ²² Dubs Rupture of Dissecting Aneurysm Simulating Perforating Gastric Ulcer Schweiz Med Wchnschr, 57, 628, 1927
- ²³ Watson, E A, and Cram, R S Ruptured Aneurysm of Abdominal Aorta Simulating Perforated Gastric Ulcer Nebraska Med Jour, 17, 303, 1932
- ²⁴ Neely, J M Ruptured Abdominal Aorta Clinico-pathologic Study of 5 Cases from Lancaster County Medical Museum Nebraska Med Jour, 22, 370-377, 1937
- ²⁵ Duchanoff Rupture of Aneurysm of Abdominal Aorta, Case Simulating Acute Renal Disease Ztschr Urol Chir 40, 34-36, 1934
- ²⁶ Rusche, C, and Bacon, S K Ruptured Abdominal Aortic Aneurysm Simulating Perinephritic Abscess, with Report of Case Brit Jour Urol 7, 330-332, 1935
- ²⁷ Willis, P W Ruptured Aneurysm of Abdominal Aorta with Left Retrorenal Hematoma, Symptoms Suggestive of Right Urethral Calculus Surg Clin North Amer, 10, 1231-1234, 1930
- ²⁸ James, T G I Uremia Due to Aneurysm of the Abdominal Aorta Brit Jour Urol, 7, 157, 1935
- ²⁹ Riggs, T F, and Massey, B D Aneurysm of the Abdominal Aorta Which Terminated with Rupture into the Duodenum Journal-Lancet, 51, 413-416, 1931
- ³⁰ Scully, F J Rupture of Aneurysm of Abdominal Aorta into Small Intestine, Case Tri-State Med Jour, 9, 1743-1744, 1936
- ³¹ Washburn, R N, and Wilbur, D L Obstruction of Duodenum Produced by Aneurysm of Abdominal Aorta Proc Staff Meet Mayo Clinic, 11, 673-677, 1936
- ³² Massary, E de, et Flandrin, P Rupture into Duodenum of Aneurysm of Abdominal Aorta, Case Bull et mem Soc med d hop d Paris, 52, 1205-1207, July, 1928
- ³³ Jaffe, H Rupture of Abdominal Aneurysm Simulating Acute Intestinal Obstruction Brit Med Jour, 1, 1173, 1925
- ³⁴ Colt, G H Aneurysm of Abdominal Aorta Brit Jour Surg, 13, 109-113, 1925
- ³⁵ Eckert, G A, and Graves, W A Abdominal Aneurysm Which Ruptured Through the Diaphragm U S Naval Med Bull, 29, 667-671, 1931
- ³⁶ Girode, Moricard, et Brouet Embolism of Aortic Bifurcation in Syphilitic with Aneurysm of Abdominal Aorta Death Following Surgical Intervention, Case Ann anat path, 10, 616-619, 1933
- ³⁷ Terakado, M Aneurysm of Abdominal Aorta with Specific Circulatory Disturbance

- in Lower Extremity, Case Bull Naval Med Assoc, Japan (Abstr Sect), 26, 3-5, 1937
- ³⁸ Croly, H G, and Graves Abdominal Aneurysm Which Ruptured Through the Diaphragm Trans Royal Acad Med, Ireland, 43, 389-391, 1894-1895
- ³⁹ Rennie, J K Abdominal Aneurysm, Case with Rupture and Formation of False Aneurysm and Extensive Erosion of Vertebrae Lancet, 2, 923-924, 1929
- ⁴⁰ Gilmour, J, and McDonald, S Aneurysm of Abdominal Aorta and Thrombosis of Superior Mesenteric Artery Associated with Bullet Wound of the Lung Brit Med Jour, 2, 587-589, 1932
- ⁴¹ Fooks, K P Abdominal Aneurysm Causing Thrombosis of Inferior Vena Cava Brit Med Jour, 1, 97-98, 1929
- ⁴² Tice, F Abdominal Aneurysm, Physical Signs with Reference to Differential Diagnosis Med Clin North Amer, 2, 673, 1917
- ⁴³ Laubry, C Radioscopy of Aneurysm of Abdominal Aorta Bull et mem Soc med d hôp d Paris, 44, 1293, 1920
- ⁴⁴ Ribadeau-Dumas et Mallet Radioscopy of Aneurysm of Abdominal Aorta Bull et mem Soc méd d hôp d Paris, 44, 1348, 1920
- ⁴⁵ McClure, C C Aneurysm of Abdominal Aorta, Case Radiology, 17, 825-827, 1931
- ⁴⁶ Unger, A S, and Poppel, M H Aneurysm of Abdominal Aorta, Case Exhibiting Annular Calcification Am Jour Roentgenol, 36, 523-524, 1936
- ⁴⁷ Brailsford, J F Aneurysm of Abdominal Aorta, Diagnosis by Lateral Radiograph of Spine Brit Jour Surg, 14, 369-371, 1926
- ⁴⁸ Kampmeier, R H Aneurysm of Abdominal Aorta A Study of 73 Cases Am Jour Med Sci, 192, 97-109, 1936
- ⁴⁹ Wedd, A M Abdominal Symptoms of Heart Disease with Special Reference to the Rôle of Auricular Fibrillation Surg, Gynec and Obstet, 45, 790, 1927
- ⁵⁰ Vallee, A Multiple Infarcts of the Spleen in Malignant Endocarditis Canad Med Assoc Jour, 9, 1964, 1919

DISCUSSION—DR ALLEN O WHIPPLE (New York, N Y) I am particularly pleased to have the opportunity of discussing Doctor Rodman's paper, because it appealed to me very much in its conception, and in discussing the matter with him during the past three or four months, I thought that the paper was particularly opportune. So far as I know, this is the first time that these various types of cardiovascular diseases, either of preoperative or postoperative lesions, have been collected and discussed in a paper before this Association.

The analysis of these various lesions and the way in which Doctor Rodman has discussed them show very definitely that he has given this matter real study in conjunction with his associates on the medical services. That brings up one of the points that I wish very emphatically to emphasize, which is the teamwork in the hospital between the man who is interested in cardiovascular disease and the surgical team. We have found it of the greatest help, both in our general surgical service and in the service on the surgery of the extremities under Doctor Darrach.

The constant help of the medical group in evaluating the operative risks in the patients, where the operation is one of choice, has been of the greatest help as well as in the patients where the question comes up as to whether to explore or not to explore, because, as Doctor Rodman has said, at times this is a most important decision. Unless the patient is operated upon, it may be a terrible catastrophe if not operated upon, or if the patient is operated upon with one of these lesions, it may be entirely contraindicated.

There are two points that I wish to emphasize. One is the advantages of oxygen therapy in some of these patients with a damaged myocardium and impaired circulation. We have been impressed with this in several groups of

cases, particularly the thyroid group, and, secondly, with the group of cases in which there is a thoracic lesion associated with the damaged myocardium.

The placing of the patient in an oxygen tent, or even better, in an oxygen room, removes a very real burden from the patient in his first two or three days after operation.

The second point which I wish to emphasize, and I am sure that the group from the Toronto Clinic will speak of this, is the advantage of heparin therapy. We have not had anything like the extensive experience that they have had in Toronto, but we have been tremendously impressed with the efficacy of heparin as a preoperative as well as a postoperative measure, in preventing thrombosis and emboli.

DR MONT R. REID (Cincinnati) I want to cite one case which will illustrate another abdominal vascular condition which Doctor Rodman did not include in his paper, namely, so-called arteritis nodosa. Recently, a young man, age 33, was sent into the hospital from the receiving ward with the diagnosis of a ruptured peptic ulcer. He was having excruciating pain and there was marked tenderness in the epigastric region. However, he did not appear to be very sick, nor did he have any muscular rigidity of the abdomen. On further questioning, it was learned he had had these pains for several weeks. The operation was deferred. The patient was then studied very carefully on both the surgical and medical services, where all kinds of roentgenologic and laboratory studies failed to reveal any organic lesion. The severe pain persisted. The medical resident, Doctor Shiro, suggested that it might be a case of arteritis nodosa. The diagnosis was eventually confirmed through a biopsy of muscle. The histologic sections of the vessels removed were typical of arteritis nodosa.

One interesting thing about this case was that the patient was given sulfanilamide with extraordinary improvement. The temperature, which had been running around 101° F. before operation, soon became normal. His pain was relieved. It has been a year since this therapy was instituted and the patient still remains apparently well.

DR ARTHUR M. SHIPLEY (Baltimore) Some years ago there came onto the service of the late Doctor Boggs at City Hospital a Negro, age 30, with a mass in the region of his right kidney. This case was worked up on the medical service and a diagnosis of perinephritic abscess was made. He had had no evidence of aneurysm of the abdominal aorta clinically. He had a large shadow which obscured the aneurysm in the roentgenogram—the aneurysm which was found later. Fortunately for the man and for myself, I used the patient in teaching a small group of students, and I went down on this mass through a small incision. When I came down to the tense area containing the supposed pus, I used a curved Kelley clamp, and showed them how to enter such an area without using a knife. When I thrust the clamp into this mass, I had to pull my head over to one side to keep the spurt of blood from hitting me in the face—then I found myself in the position of the small Dutch boy who stuck his finger in a hole in the dike, and I wondered what I should do next. I introduced a number of sutures around my finger and had the assistant tie these one after the other and finally withdrew my finger without the occurrence of further hemorrhage. Four months later the man died. He had a small aneurysm of his abdominal aorta which had slowly perforated, and what he had also was a secondary surgical aneurysm which simulated, clinically, the findings in a perinephritic abscess. Of course I know what I should have done, I should have put an aspirating needle into this area before using it for a teaching demonstration, and that was a sin of omission which I have not forgotten.

DR HARVEY B. STONE (Baltimore) It has been said that science consists in the discovery, the verification and the classification of facts. Certainly, I think Doctor Rodman's contribution should be considered a valuable scientific achievement from the standpoint of grouping into a coherent, organized classification these vascular lesions which we, of course, have all known about and worried about for a long while.

I think anyone who is actively engaged in teaching must feel very grateful to Doctor Rodman for presenting this nicely grouped and correlated study of these very important and very confusing conditions. Certainly, for me it will be a much easier task to bring sharply and definitely to the attention of students these various forms of cardiovascular lesions which may be confused with surgical conditions.

I think another thing stands out very clearly from this careful grouping, which is, that of all the various conditions described by Doctor Rodman, one group only requires surgical intervention, namely, embolic or thrombotic lesions involving the blood supply of the intestine, and this sharply distinguishes, from the standpoint of therapy, this one out of all the other vascular complications which may occur.

I suppose every one of us, perhaps, could cite instances in which he has made mistakes either in operating upon a supposed surgical condition which turned out afterward to be a vascular lesion, or the reverse error of failing to operate in the belief that the condition was a vascular lesion but which actually was a surgical condition.

There is one case that I should like to cite which was not covered in Doctor Rodman's very comprehensive recitation indicating the complications that may occur with abdominal aneurysms. In brief, the patient came in with a history of sudden severe shock rendering him unconscious. He was found lying on the ground. Some hours later, he was seen in the hospital by me, and I was unable to make a definite decision as to what was wrong with him. I asked Dr. William Fisher to see him with me, and after considerable uncertainty, we decided that he probably had an acute pancreatitis. I shall not go into his symptoms except to say that they did simulate very closely those of acute, fulminating, hemorrhagic pancreatitis. I explored him and found a pancreas greatly distended and swollen and filled with blood, some free blood in the abdominal cavity, but it was noticed at operation that there was no evidence of fat necrosis. He was simply drained, the wound closed, and he died a few hours later. He had a dissecting aneurysm of the abdominal aorta which had ruptured into the pancreas.

DR WILLIAM E. GALLIE (Toronto, Canada) I have been injected into this discussion by Doctor Whipple without any previous intention on my part of appearing. I can say, however, that the clinical experiences with heparin, which were reported before this society last year by Doctors Murray and Best, have continued to be most encouraging, and that now a very considerable number of patients with emboli lodging in the great vessels, such as the bifurcation of the aorta into its iliac branches, have been dealt with successfully by the removal of the embolus and subsequent treatment with heparin.

Perhaps more important than these cases of arterial embolism, have been a series of four cases of thrombosis of the mesenteric vein, in which excision of the gangrenous bowel followed by the administration of heparin has resulted in the prompt recovery of the patients without the usual extending thrombosis which almost always terminates these cases. We are naturally enthusiastic, therefore, regarding the usefulness of this drug.

MEMOIRS

EMMET RIXFORD

1865-1938

IF TWENTY years or so ago one mentioned San Francisco to a group of doctors, instantly, together with pictures of the Golden Gate and the great earthquake and fire, there would come to their minds the figure of Dr Emmet Rixford. Doctor Rixford was a part of the West and the West was his. He knew it, he loved it, he helped build it. He walked over it, sailed over its waters, slept under its open skies, climbed its mountains, stood under its trees. He knew its old builders, both the great and the lowly. He talked with them and listened to their stories and told them some of his own, he took care of them and helped relieve their sufferings when they were sick. He knew Western trees and plants and flowers, knew them intimately, he knew the animals and rocks.

Doctor Rixford was born February 14, 1865, in Bedford, a small town in Canada near the Vermont border. His father was a Vermonter, his mother Canadian. His family made axes and scythes in two factories, one in East Highgate, Vermont, and the other in Canada. In 1867, when he was two years old, his parents set out for California in a "side-wheeler," crossed Nicaragua and settled in San Francisco. His father secured a position with the San Francisco Bulletin and was later in the employ of the State Department of Horticulture. Doctor Rixford inherited his love of nature from his father.

He attended the San Francisco public schools and entered the University of California as a student of engineering, graduating in 1887. He often said that his engineering studies had stood him in good stead during his practice of surgery, and had helped him especially to understand the mechanics of fractures, a subject to which he gave particular attention. After having graduated in engineering, he decided to become a doctor and enrolled in the classes of Cooper Medical College, from which he received his doctor's degree in 1891. Among his teachers was Dr L. C. Lane, a former Navy Surgeon, a Greek and Latin scholar, and the best known surgeon on the Pacific Coast. Lane's clear, cold, classic intellect attracted the young student and after his graduation he became Lane's assistant. He helped him at operations and often acted as nurse and orderly to his patients afterwards. Lane had a busy office in the older business portion of San Francisco, the upper stories of the building were equipped as a small hospital, and here, Doctor Rixford, who had helped operate upon the patients by day, used to take turns with other young men in watching over them at night. Lane never mastered asepsis. He used to consider operation for inguinal hernia unjustifiable, but he was a cool and brilliant operator.

In 1896, Doctor Rixford met Sir William Macewen, of Glasgow, who had come to San Francisco to deliver the first course of Lane Lectures, and ever



EMMET RINFORD, M D

after the influence of Macewen's dominating mind was detectable in his speech and acts

In 1892, soon after receiving his degree, Doctor Rixford left for the East and spent a year as resident at the New York Hospital for Ruptured and Crippled under the elder Coley. During the summer of 1892, he worked at the Johns Hopkins Hospital in Welch's laboratory. In 1893, he returned to San Francisco and set out to practice surgery on his own account. He was made Adjunct Professor of Surgery at Cooper Medical College in 1893, and Professor of Surgery in 1898.

His publications and his active participation at society meetings and in discussions soon gained him national recognition. He was elected Vice-President of the American Surgical Association in 1905, and was its President in 1928. In this same year, at the request of Dr. Harvey Cushing, he served as Surgeon in Chief, *pro tem*, of the Peter Bent Brigham Hospital in Boston. He was a member of the Society of Clinical Surgeons and attended their foreign tours regularly. He was a founder of the Pacific Coast Surgical Society and its President in 1932. He belonged to many other societies and held many other offices.

His earlier publications deal with all kinds of surgical topics: hernia, goiter, pancreatitis, gallstones, cancer, etc. His most enduring work will probably be the paper in Vol. 1 of the Johns Hopkins Hospital Reports, in which he recognized and, together with Gilchrist, described a new disease, coccidioidal granuloma, and a number of papers on the mechanics and production of fractures, in which he described the physical principles underlying the production of torsion, flexion, buckling and green stick fractures.

The bald recital of his scientific achievements and honors can give but an incomplete idea of this man. His advice and help were sought by patients and colleagues from all over the Pacific Coast. His clinics and colloquia were academic presentations such as few men could offer. Lane Library, the largest medical library in the West, stands as a lasting monument to his love for books and learning. His knowledge of the medical history of the Pacific Coast was wide and accurate. Many of his best writings deal with Western medical history and biography. One regrets that he did not write more of himself, for his hand, no less than Lane's and Cooper's and Toland's, of whom he wrote, guided Western medicine. He knew many of the old pioneers himself, he was close enough to their life, their works and their times to write of them vividly, accurately, understandingly and with justice.

Like these older predecessors of his, he occupied himself with natural history in general and not only with the natural history of disease—inescapably for one who turns to medicine as the most natural avenue for the exercise of an inquiring and logical mind, but who finds it impossible to shut his eyes to the many objects with which a new country surrounds him. He was a true outdoor naturalist, with companions, later with his children, he made pack trips into the Sierra Nevada Mountains and, as he walked, studied the untouched world around him. He climbed the peaks, Mt. Rixford, a 13,000-foot

peak of the Kearsarge Range, is named for him. His early engineering days had awakened in him a peculiar fondness for the snail. He was fond of studying this curve wherever he met it, and so, in his later years, he collected the shells of land snails and grew to be an authority on them. His town house and his garden, quite near the busy automobile section, were a museum of natural history and an experimental station. After his retirement from teaching, at the age of 65, he found more time for gardening, like his father, who, at the age of 90, began to hybridize orchids that took ten or 20 years to germinate, he went at it with profound interest and zeal. He helped organize the State Horticultural Society and he covered his country place at Los Altos with roses, which he crossed, grafted and raised from seed. He supplied parks and botanical gardens with roses of the original primordial stock which he grew from seed sent him from various countries of Asia.

Doctor Rixford was not a sportsman in the ordinary sense. His thrifty Vermont lineage, I suppose, forbade that, but also his turn of mind, which would rather watch and note the actions of his fellow men and other animals, than struggle with them or kill them. He liked the sea, however, he owned and sailed a large old sloop—the *Annie*. The *Annie* was built in New York in the 70's, and had been a fast sailer in her day. There was a not too well exploded legend that she had been used to convey Boss Tweed from New York to safer quarters when a retreat seemed judicious. Parties of younger doctors and hospital interns, and later his children, manned her until she got too decrepit, when her skipper had her burned at sea rather than let her rot in the mud.

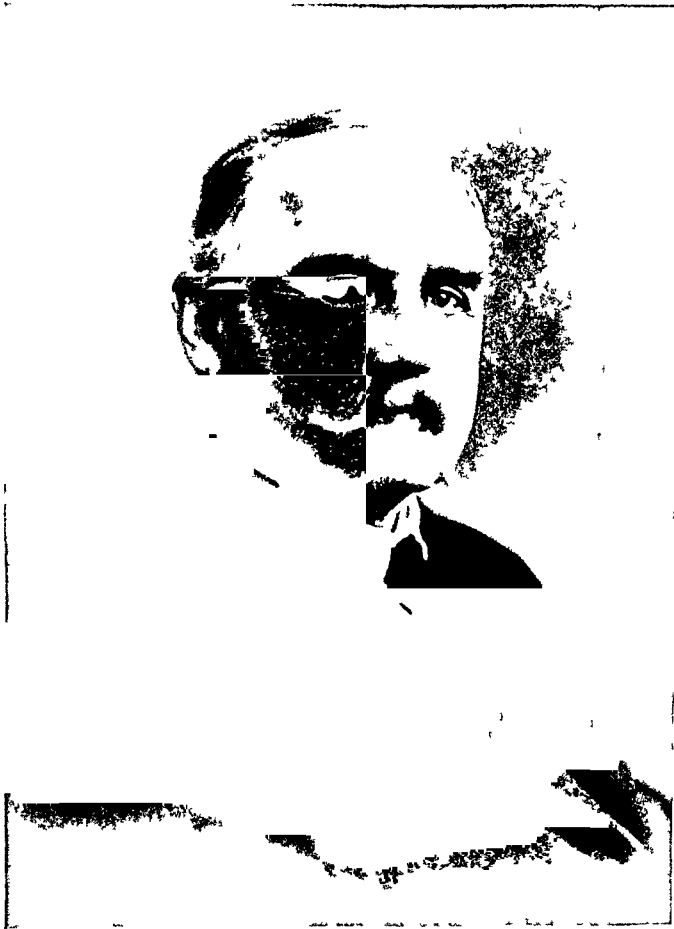
Toward the end of 1937, Doctor Rixford, still vigorous and giving promise of many useful and active years, discovered signs of a carcinoma of the bladder. He died in Boston following a surgical operation, January 2, 1938. His was an unusually varied, useful and active life. He combined the broad interests for all manner of natural phenomena that were characteristic of the best of the earlier American scientists and surgeons with an inquiring, analytic and logical mind, with a retentive, historical and judicious memory and with truly academic learning.

LEO ELOESSER

SIR THOMAS MYLES

1857-1937

IN THE death of Sir Thomas Myles, an honorary fellow of the American Surgical Association, Ireland has lost one of its most outstanding surgeons. Sir Thomas was well known to many of the members of the American Surgical Association, since he had visited in this country on a number of occa-



SIR THOMAS MYLES, M.D.

sions, and had made important contributions to the scientific sessions of the Association. Those who had the opportunity of visiting him in Dublin and attending his surgical clinics will always remember him as a great surgeon and teacher and will recall his inspiring personality.

Sir Thomas, son of John Myles of Limeick, was born April 20, 1857. He studied medicine at Trinity College, Dublin, where he received his M.B. and B.Ch. in 1881 and in 1889 his M.D. He served as house surgeon at Steevens Hospital and, in 1885, became a Fellow of the Royal Chirurgical Society of Ireland and was appointed secretary of the Dublin Hospitals Commission. In 1889, he was appointed professor of pathology at the Royal

College of Surgeons of which he was President from 1900 to 1902. For many years he was visiting surgeon to Jervis Street Hospital and later to Richmond Hospital, where the remainder of his active professional life was spent. In 1900, he was made honorary burgess of his native city of Limerick and received the honor of knighthood in 1902. He represented his college on the General Medical Council from 1905 to 1911 and from 1933 until the time of his death. In 1910, he was appointed honorary surgeon in Ireland to King George V, and during the World War, Sir Thomas served as a consulting surgeon to the forces in Ireland. He was elected to honorary membership in the American Surgical Association in 1907. He passed away at his home in Leeson Park, Dublin, July 14, 1937.

The eulogies appearing in the medical journals of Great Britain and Ireland depict Sir Thomas as a man of rare personal charm, equanimity and high scholarly attainments. Sir Thomas possessed a profound knowledge of the surgery of his time and his originality was displayed in many of the contributions by which he advanced surgical progress. He was a man of magnificent physique who was seen by one writer as one who had discovered the secret of perpetual youth. He was most tolerant of the opinions of others and, as another writer has expressed it, "I never saw him out of temper," and "he never forgot a friendly act nor desired to remember an unfriendly one."

I take the liberty of quoting in part a tribute to Sir Thomas from his lifelong friend, Mr. A. B. Mitchell, of Belfast. "Sir Thomas Myles was an outstanding personality in any company. His conversation was always fascinating because of the extraordinary range and accuracy of his knowledge and the simplicity and forcefulness with which he expressed himself. His acquaintance with history was profound. He was one of our greatest Shakespearean scholars, and constantly quoted his favourite author with a fervour and suitability that was most impressive. He was endowed with a colossal memory. He was a voracious reader. A book once read was mastered, he could refer to its individual characters years afterwards as if he had lived and moved amongst them. His wonderful capacity as a teacher of medicine and surgery will never be forgotten till his last pupil has gone to join him in the 'Everlasting Land.' It is not too much to say that one's first visit to 'Tom Myles' Ground' was a revelation. The lucidity, brevity, accuracy, and virility of his descriptions of disease were altogether unique. He prepared more than 1,000 young men for various medical degrees, and for entrance examinations for the Army, Navy, and Indian Medical Services. His pupils have attained the foremost positions in every part of the British Empire. Wherever they went they carried with them not only profound admiration but a deep affection for their great teacher. It is impossible to overestimate his influence upon the lives and character of those who came under his magnetic personality."

The American Surgical Association honors the memory of Sir Thomas Myles and is honored to have on its roster the name of this distinguished surgeon of Ireland.

DONALD C. BALFOUR

JOHN LAWRENCE YATES

1872-1938

JOHN LAWRENCE YATES, who died at his home in Milwaukee, November 3, 1938, of an acute throat infection, was born in Milwaukee, Wisconsin, February 27, 1872, the son of Theodore and Marion Wolcott Yates. Doctor Yates was graduated from the Phillips Exeter Academy in 1891, after which



JOHN LAWRENCE YATES, M.D.

he attended the Sheffield Scientific School of Yale, receiving the degree of Ph.B. in 1894. He then did postgraduate work for a year at the University of Wisconsin where he received the degree of B.S. in 1895. He was graduated from the Johns Hopkins Medical School in 1899, and was for some time subsequently an assistant in Pathology at that institution. In 1901, he became assistant demonstrator of Pathology at the University of Pennsylvania under Dr. Simon Flexner. Following this, he was for some time associated with Dr. Albert Ochsner at the Augustana Hospital in Chicago and, in 1906, began the private practice of surgery in Milwaukee, Wisconsin, which he continued

until the time of his death. In 1905, he married Katherine Gross, of Harrisburg, Pennsylvania, who, with his sister, Miss C M Allis, survive him. At the time of his death he was on the surgical staff of several hospitals in Milwaukee and was associate research professor of Oncology at the University of Wisconsin and the Marquette University Medical Schools. He was for many years a fellow of the American Surgical Association, a member of the Association of Thoracic Surgeons, the Society of Clinical Surgeons and many other medical and surgical societies, local and national.

From the above, it is evident that he had led a most active and productive professional life which had earned for him the reputation of being one of America's outstanding surgeons. From his earliest days, he had an unquenchable thirst for investigation of the unknown and this spirit of research influenced and directed all of his professional life. Unlike many interested in research, he was also keenly interested in the human and clinical side of surgery and was devoted to the welfare of his patients, and they in turn devoted to him. No personal sacrifice was ever too great if thereby someone might be benefited. In some of his researches he used himself as an experimental animal and upon one occasion in particular seriously impaired his health. For years he studied and wrote about Hodgkin's disease and related disorders. He made many contributions to surgical literature, notably in connection with the use of drains in peritonitis which he devised, the treatment of gunshot wounds of the chest and latterly cancer, in which he strove to demonstrate the existence of antigens and antibodies. Immediately upon the entrance of the United States into the World War he joined the Medical Corps and ultimately was commissioned a Lieutenant Colonel. He was deeply interested in the treatment of gunshot wounds of the chest and in the quiet periods carried on investigations along these lines in the United States Laboratories at Dijon, but during periods of activity he was always functioning as a surgeon as near the front lines as he was allowed, and to him were usually allotted the bad chest wounds which he handled most skillfully and effectively and taught many others so to do. He was a most patriotic individual and never could quite forgive those whom he thought had slacked their job.

He was possessed of a most charming personality, seriously earnest in everything he undertook but tempered with a joyous nature and a genuine sense of humor which always relieved the drab spots. No one, and they are many, who has ever heard his hearty laugh will forget it. Wherever he went he spread joy and mirth and he was a glorious companion in fun or fight, and the latter he could do when he felt a cause or condition demanded it. His happy nature gave him a cheerful outlook upon life and greatly enhanced his value to his patients, many of whom were cured of their maladies quite as much by his cheery, optimistic manner as by his surgical skill, and the combination was well-nigh perfect.

Honesty, intellectual and actual was one of his most outstanding qualities and when one asked him a direct question, he received a direct answer.

Loyalty was another superb quality possessed by him in a striking manner.

and never in his life did he fail a friend in time of need. Of his great industry mention has already been made and he played, when he did play, quite as hard as he worked—and he was a grand playboy. To his great host of friends, lay and professional, he was known as “Jack,” which perhaps indicates in some fashion their feeling for him. Rarely, among the host of those who knew him, was he called Doctor Yates but rather Jack Yates. Honesty, Loyalty, Industry, Courage and Ability may be said to have been his outstanding characteristics.

A life full of service to his fellow man, well and effectively lived, he has left a definite impress upon American surgery which will live on, but in the hearts of his patients and many friends, a void that can never be filled.

ARTHUR W. ELTING

EDWIN BEER

1876-1938

EDWIN BEER was born in New York City in 1876. He was graduated from Columbia College in 1896, and three years later received his medical degree from the College of Physicians and Surgeons of New York. Upon the completion of his internship at the Mount Sinai Hospital, he went abroad



EDWIN BEER, M.D.

to complete his postgraduate studies in the clinics of Prague, Berlin and Vienna. Shortly after his return to New York, he became associated with the Mount Sinai, Bellevue, Flower, Neurological and the Lenox Hill Hospitals. It was at this latter institution that he developed one of the first cystoscopic departments in the city. In 1910, he was appointed an attending surgeon to the Mount Sinai Hospital and, although in charge of a general surgical service, he became more interested in the field of urology. He served in France during the World War as a Lieutenant Colonel in the U. S. A. Medical Corps. He was a fellow of the New York Surgical Society and its

President upon the occasion of its fiftieth anniversary. He enjoyed fellowship in the American College of Surgeons, the American Urological and the American Surgical Associations, and the International Society of Surgeons. He was a Vice-President of the New York Academy of Medicine and a President of the Medical Board of the Mount Sinai Hospital.

In 1938, upon the occasion of his sixty-second birthday, he was presented with an anniversary volume containing over 70 presentations contributed by his many friends both here and abroad. Although seriously ill at the time with a malady which was to cause his death on August 13, 1938, this volume brought him great joy.

Edwin Beer's medical contributions were innumerable and covered not only the more important problems in many branches of surgery, but especially urology. He was greatly interested in the urologic diseases in the young and perfected one of the first practical cystoscopes for infants. In 1930, he published a monograph on Disease of the Urinary Tract in Children. This was an exhaustive treatise based upon the modern methods of urologic investigation. The crowning event in his brilliant career came in 1927 when, at Brussels, he received the first gold medal given by the International Society of Urology for the use of the Oudin high frequency current in benign bladder tumors, a method which revolutionized their treatment. In 1937, he was awarded the Gold Key by the American Congress of Physical Therapy for his outstanding contributions to the treatment of vesical tumors. His unusual experience in this field enabled him to write an invaluable monograph on Tumors of the Urinary Bladder, which was published in 1937.

Edwin Beer was a born scholar, endowed with a magnificent intellectual background which gave him an unusual clarity of thought whether in surgery or in the field of economics or sociology. He was a great teacher and his surgical approach to any problem was marked with meticulous attention to the slightest detail, a characteristic which could not help but impress those about him. He was a mental stimulus and an inspiration to the younger generation of surgeons, who came to rely upon his judgment and advice. His untimely death deprived surgery and urology of one of its great original minds.

RALPH COLP

FRANZ J A TOREK

1861-1938

FRANZ J A TOREK was born April 14, 1861, in Bieslau, Germany. At the age of 11, he came to America with his parents and attended the public schools and later the College of the City of New York, graduating at the age of 19. He was elected to Phi Beta Kappa. After teaching English for sev-



FRANZ J A TOREK, M D

eral years, he studied medicine at the College of Physicians and Surgeons and received the degree of M D in 1887.

Following graduation, he served an internship at the German Hospital, now the Lenox Hill Hospital, and remained connected with it until his death, a period of over 50 years. He was a member of the Attending Staff of the New York Post Graduate Hospital, from 1890 to 1915, when he resigned after 25 years of service. He was attending surgeon at St. Mark's Hospital from 1891 to 1905. The history of the New York Skin and Cancer Hospital is closely interwoven with the name of Doctor Torek, for he served on the

Attending Staff from 1890 to 1935, during almost the entire period of independent existence of that institution. After it became merged with the New York Post Graduate Hospital, he was appointed Consulting Surgeon.

He was a member of leading medical and surgical societies, including in addition to the American Surgical Association, the New York Surgical Society, the New York Society for Thoracic Surgery, the American Association for Thoracic Surgery and the German Medical Society. He was an Ex-President of the three latter organizations.

Doctor Torek was a versatile general surgeon. There is no field of surgery into which he did not venture and to which he did not make some worthwhile contribution. Especially, operations requiring technical skill interested him, and this is evident in his writings. The different procedures he developed were always the result of careful planning and practice on the cadaver. His approach to a difficult surgical problem was likewise one of detailed planning and then executing it with an ease and skill which made it appear almost simple. His unusual talents found their greatest application in his treatment of cancer, in which his patience, his deftness and his courage were of inestimable value. Although his publications in this field are limited, it is perhaps principally for his radical cancer operations that he will be remembered by those who were associated with him. His chief service to the public lies in the relief or cure afforded innumerable sufferers from cancer.

His service to the profession may be measured by the training of numerous young surgeons, who were associated with him during the course of years, to be good cancer surgeons. A radical procedure, carried out with neatness and attention to detail, was the point he stressed.

Several operations he developed indicate original thoughts on the subject, and when he presented them they were supported by abundant clinical material.

In 1919, he reported an operation for inguinal hernia, based on the observation that the sac always descends between the vas and vessels of the cord. By high ligation of the neck of the sac and by separating these two structures with the aid of two or three sutures, he sought to overcome this tendency. He was so well satisfied with the method that he continued it throughout his life.

The Torek operation for undescended testicle is being practiced with increased frequency by surgeons throughout the country.

His outstanding contribution to surgery is the operation for carcinoma of the thoracic portion of the esophagus. In November, 1914, he presented the first successful resection. This case has remained famous in the surgical literature because cure resulted and the patient lived for more than 12 years and finally died at the age of 79, of pneumonia. The principles underlying the operation are recognized as fundamental and are being followed by surgeons throughout the world.

In the treatment of his patients, Doctor Torek embodied all the virtues of

a great surgeon, for he had sympathetic understanding of their mental as well as their physical suffering and he tried to alleviate both

He had a musical background and was himself an accomplished musician, which contributed much to enrich his life

Doctor Toiek died in Vienna, September 19, 1938, while on a vacation trip undertaken in the hope of finding relief from a cardiac condition. He is survived by his wife, the former Minnie Volkening, and a son and a daughter, as well as several grandchildren

Because of his personality, his sterling character, his work and his contributions, Doctor Toiek will long be remembered and be an inspiration to those who follow after

He was one of America's great surgeons

CARL EGGERS

BOOK REVIEW

OPERATIVE ORTHOPEDICS By WILLIS C CAMPBELL, M D 1154
pages with 845 illustrations C V Mosby Co , 1939

Doctor Campbell's book is a notable contribution to the literature of the modern operative treatment of orthopedic conditions. The author has classified and described the commonly employed operations. The indications and technics are given in full.

He has filled a long felt need for a book to which the busy surgeon can refer for concise descriptions of the various operative technics which can be applied to the condition with which he is confronted.

The choice of the material included in the book is excellent although a number of operations which have proven to be very satisfactory, in the hands of other surgeons, have been omitted.

The 38 pages devoted to surgical approaches make this book a necessity in the library of every orthopedic surgeon.

ROBERT L PRESTON

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M D
1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English

Exchanges and Books for Review should be sent to James T Pilcher, M D , Managing Editor, 121 Gates Avenue, Brooklyn, N Y

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa

ANNALS OF SURGERY

VOL 110

NOVEMBER, 1939

No 5



SYMPOSIUM ON ANESTHESIA

PRESENTED BEFORE THE AMERICAN SURGICAL ASSOCIATION, HOT SPRINGS, VA,
MAY 11, 12, 13, 1939

THE INFLUENCE OF CERTAIN DRUGS AND ANESTHETICS ON GASTRO-INTESTINAL TONE AND MOTILITY

J DEWEY BISGARD, M D, AND E K JOHNSON, M D, OMAHA, NEB

THE ASSAY OF ANESTHETIC AGENTS

HENRY K BEECHER, M D, BOSTON, MASS

TRENDS IN INHALATION ANESTHESIA

WESLEY BOURNE, M D, MONTREAL, CANADA

ANOXIA A SOURCE OF POSSIBLE COMPLICATIONS IN SURGICAL ANESTHESIA

R D McCLURE, M D, F W HARTMAN, M D, J G SCHNEDORT, M D,
AND V SCHELLING, PH D, DETROIT, MICH

THE PRESENT STATUS OF SPINAL ANESTHESIA

HAROLD L FOSS, M D, DANVILLE, PA

THE EVOLUTION OF SPINAL ANESTHESIA IN ABDOMINAL SURGICAL PROCEDURES

ROSCOE R GRAHAM, M D, TORONTO, CANADA

FURTHER EXPERIENCES IN THE USE OF SPINAL ANESTHESIA FOR THORACOPLASTY

F B GURD, M D, A M VINEBERG, M D, AND WESLEY BOURNE, M D
MONTREAL, CANADA

INTRAVENOUS AND REGIONAL ANESTHESIA

JOHN S LUNDY, M D, ROCHESTER, MINN

THE USE OF SYMPATHETIC NERVE BLOCK ANESTHESIA IN MINIMAL RESECTION OF THE STOMACH FOR ULCERS OF THE PYLORIC ANTRUM AND DUODENUM

WILLIAM F RIENHOFF, JR, M D, BALTIMORE, M D

TRANSACTIONS

OF THE

AMERICAN SURGICAL ASSOCIATION

MEETING HELD AT HOT SPRINGS, VA

MAY 11, 12, 13, 1939

(Continued)

THE INFLUENCE OF CERTAIN DRUGS AND ANESTHETICS UPON GASTRO-INTESTINAL TONE AND MOTILITY*

J DEWEY BISGARD, M D , AND E K JOHNSON, M D

OMAHA, NEB

FROM THE DEPARTMENTS OF SURGERY AND PHYSIOLOGY, UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE OMAHA, NEB

POSTANESTHETIC and postoperative disturbance of gastro-intestinal activity manifests itself by nausea and vomiting, by distention from gastric and intestinal dilatation and by gas-pains. With the exception of the immediate postoperative nausea and vomiting, the signs and symptoms of gastro-intestinal dysfunction are attributed by most pharmacologists and surgeons solely to factors unrelated to anesthesia, such as operative trauma to tissues, toxemia, "air swallowing," and postoperative medication. Disturbances resulting from such complications, as mechanical pyloric and intestinal obstruction and ileus associated with peritonitis, are excluded from this discussion.

Unquestionably, surgical trauma is the principal causative factor of postoperative gastro-intestinal symptoms, but the results of the clinical and experimental studies which follow indicate that anesthetics play much more important rôles than are generally attributed to them. These studies also show that some anesthetic agents are inhibitory and others are predominantly motor stimulating to the gastro-intestinal tract, and that those with inhibitory action are associated with disturbances of gastric and intestinal functions much more frequently and that the symptoms of such disturbances are, on the whole, more severe and of longer duration. Also from the studies, there evolved some evidence that the differences in the effects of the two types of anesthetic agents upon the gastro-intestinal tract may be related to their respective influences upon the oxygen saturation of the blood.

As recorded in Table I, an analytic study was made of 408 cases which had had celiotomies with uncomplicated convalescences. These cases were per-

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

sonally observed, either directly or indirectly, and specific records of nausea and vomiting, distention and "gas-pains" maintained and accumulated for the purpose of this study

The tabulated results show a very impressive difference in the response of gastric and intestinal activity to the various forms of anesthetics indicating the important rôle played by these agents. Sixty-one per cent of cases operated upon with avertin (60 to 90 mg per Kg of body weight) -cyclopropane anesthesia never vomited following operation as compared with only 4 per cent with ether, 4.5 per cent with nitrous oxide and ether, 10 per cent with nitrous oxide alone, 20 per cent with cyclopropane alone and 32 per cent with spinal. Similarly, vomiting persisted longer than 24 hours in only 1.3 per cent of cases anesthetized with avertin-cyclopropane as compared with 10 per cent with ether, 14 per cent with nitrous oxide-ether, and 2.2 and 2 per cent with spinal and cyclopropane alone, respectively. There was slight or no distention with avertin-cyclopropane in 50 per cent of cases as compared with only 27 per cent with ether, 30 per cent with nitrous oxide alone or with ether, 40 per cent with spinal and 25 per cent with cyclopropane alone. Distention was persistent and troublesome in no case which received avertin-cyclopropane, in only 1 per cent of cases given spinal anesthesia and in 3 per cent given ether alone or in combination with nitrous oxide. Persistent and troublesome gas-pains occurred in only 1.3 and 2.3 per cent of cases given avertin-cyclopropane and spinal anesthesia, respectively, as compared with 10, 9, 8, and 3 per cent in those given nitrous oxide, nitrous oxide-ether, cyclopropane and ether, respectively. Thus it is apparent that the addition of avertin greatly reduced the symptoms of gastric and intestinal dysfunction and that spinal anesthesia exerted only slightly less favorable influence than did avertin-cyclopropane.

There are, however, a few misleading facts. Nausea and vomiting which occurred in the operating room and before the patients returned to their rooms was not recorded. Consequently some cases credited as never having vomited retched or vomited in the operating room. Included are a few cases given spinal anesthesia, which vomited during operation, and several given gas anesthesia, which vomited upon regaining consciousness in the operating room. However, this included no cases which received cyclopropane as a supplement to a basal anesthesia of avertin and it is in this group that the least disturbance of gastric and intestinal activity occurred.

Also misleading is the fact that there were many children in the groups which received ether, nitrous oxide and combined nitrous oxide and ether. Since children vomit with less provocation and more persistently than adults, the figures in these groups are disproportionately unfavorable. Also, children, as a rule have less distention and gas-pains postoperatively, giving disproportionately favorable figures in this respect in these same groups.

Aside from these minor discrepancies, the cases in the various groups were relatively comparable and received comparable operative trauma and pre-

TABLE I
CORRELATION OF TYPE OF ANESTHESIA WITH SIGNS AND SYMPTOMS OF GASTRIC AND INTESTINAL DYSFUNCTION IN
408 CASES WITH UNCOMPLICATED CELIOTOMIES

Anesthetic	Cases	Nausea and Vomiting*					Distention					Gas Pains			
		None	Per Cent	Less Than 12 Hrs	Per Cent	Gas- tric Drain age	Per Cent	Per sist- ing After 24 Hrs	Slight or None	Per Cent	Mod- erate	Per Cent	Slight or Mod- erate	Per Cent	Severe Per Cent
Ether	72	3	4	46	64	23	32	7	10	20	27	50	70	2	3
Nitrous oxide oxygen	10	1	10	6	60	3	30	0	0	3	30	7	70	0	10
Nitrous oxide plus ether	65	3	4.5	45	69.5	17	26	9	14	20	30	43	67	2	3
Cyclopropane	102	21	20	62	62	18	18	2	2	25	25	73	73	2	2
Spinal-novocain, pantocaine	85	28	32	64	58.5	8	9.5	2	2.2	34	40	50	59	1	1
Cyclopropane plus avertin	74	45	61	24	32.5	5	6.5	1	1.3	37	50	37	50	0	0
Totals	408														

* Patients vomiting more than two or three times and longer than ten hours placed routinely on continuous gastric drainage (suction)

and postoperative care Since the differences in the late as well as early symptomatic manifestations of dysfunction were so great, it would appear that anesthesia exerted a prolonged as well as transitory influence upon the gastro-intestinal tract

Experimental Data—Direct observations of gastric and intestinal motor activity were made during, and for varying periods following, anesthesia in both humans and dogs

Activity of the stomach and bowel was recorded upon continuous kymographic records which registered pressure changes upon inflated balloons fastened to the ends of indwelling Levine tubes In the human subjects, the tubes (double Miller-Abbott) were swallowed and were retained either in the stomach or permitted to pass into the small bowel The location of the tubes was determined radiographically

In the dogs, the tubes with their balloons were passed into permanent fistulae of the stomach, small intestine and colon The stomach was entered through a long tube fashioned from its greater curvature (Pavlov pouch), the large bowel through an appendicostomy and the small bowel through an ileostomy leading into a Thery-Vella type of isolated loop of ileum Records were made during (1) a preanesthetic control period, (2) induction of anesthesia, (3) full surgical anesthesia, (4) a recovery period of one hour or more, and (5) varying postanesthetic intervals, some extending over periods of three days

Since the muscular activity of the gastro-intestinal tract normally varies greatly from day to day and from minute to minute, the changes in tone and peristaltic activity which take place during a period of experimental observation can be interpreted as responses to experimental factors only if they are constantly repeated under the same circumstances

Studied were the actions of a few representative drugs used in the pre- and postoperative care of patients and a few representative anesthetic agents The results are summarized under their respective headings

I Motor Effects

(1) Morphine—16 mg subcutaneously (Chart I)

(a) Man The action of morphine upon both the stomach and small bowel was constantly motor in three observations In each viscus there was a marked increase of tone, in the stomach an increase in the frequency and amplitude of peristaltic contractions and in the small bowel a diminution of amplitude The effect became apparent in approximately five minutes and after 30 minutes slowly regressed to assume relatively normal tone and activity within an hour after administration

(b) Dog In two dogs, observations of the stomach, ileum and colon were made simultaneously Both animals vomited within five minutes, the retching being immediately preceded by an increase in gastric tone and muscular activity The tone remained increased for two hours Gastric con-

tractions were greatly diminished in both frequency and amplitude for approximately two hours and were still somewhat diminished six hours after administration of the drug. Both small bowel and colon showed the same effects, namely, increased tone and diminished muscular activity, but in both there was an earlier return to normal, the ileum in three hours and the colon in two hours.

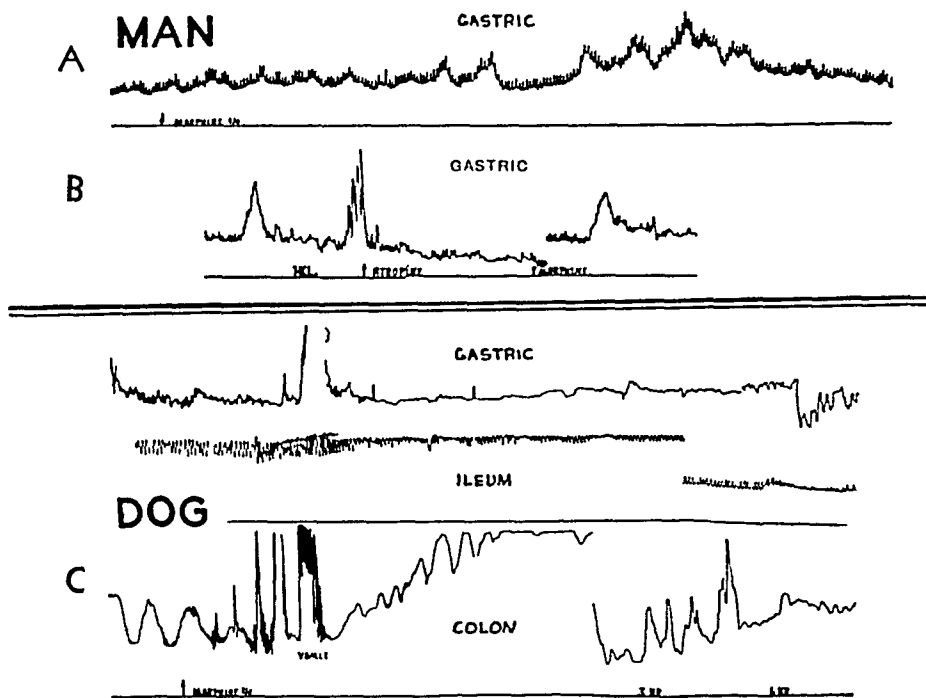


CHART 1—(A) Action of morphine (16 mg) upon a normal fasting human stomach. Note progressive increase of tone and of frequency and amplitude of contractions. (B) After inducing hunger contractions by administration of dilute hydrochloric acid to a fasting human stomach atropine (0.65 mg) caused relaxation and inhibition. Following administration of morphine (16 mg), the effect of atropine was counteracted and normal tone and contractions reestablished. (C) Simultaneous records of stomach, ileum and colon of dog showing normal tracings before morphine (16 mg) was given subcutaneously, exaggerated excursions accompanying vomiting following its administration, and then the progressive increase in tone with diminution of frequency and amplitude of contractions. Observations three and six hours later show normal tone but still diminished contractions.

(2) Pitressin—ten minims to 1 cc subcutaneously (Chart 2)

(a) Man. In three subjects, pitressin caused a great increase in both frequency and amplitude of the peristaltic contractions of the stomach but no change in tone. After a brief preliminary lessening of tone and activity both tone and peristalsis were greatly increased in the ileum and the amplitude of the rhythmic contractions was diminished. The effect lasted not longer than 20 minutes.

(b) Dog. The stomach was uninfluenced and the small bowel showed an increase of tone only. In the large bowel both tone and peristalsis were definitely increased. As in man the effect was of short duration.

(3) Dilute hydrochloric acid—20 minims orally (Chart 2)

(a) Man. In three of four patients dilute hydrochloric acid excited the fasting stomach to increased activity, both in respect to frequency and amplitude of peristaltic contractions.

II Inhibitory Effects

(1) Atropine—Charts 3 and 5

(a) Man—0.65 mg subcutaneously In both stomach and small bowel there was a marked diminution of tone and of the frequency and amplitude of contractions for approximately an hour and one-half For 30 minutes peristalsis was entirely abolished in the ileum

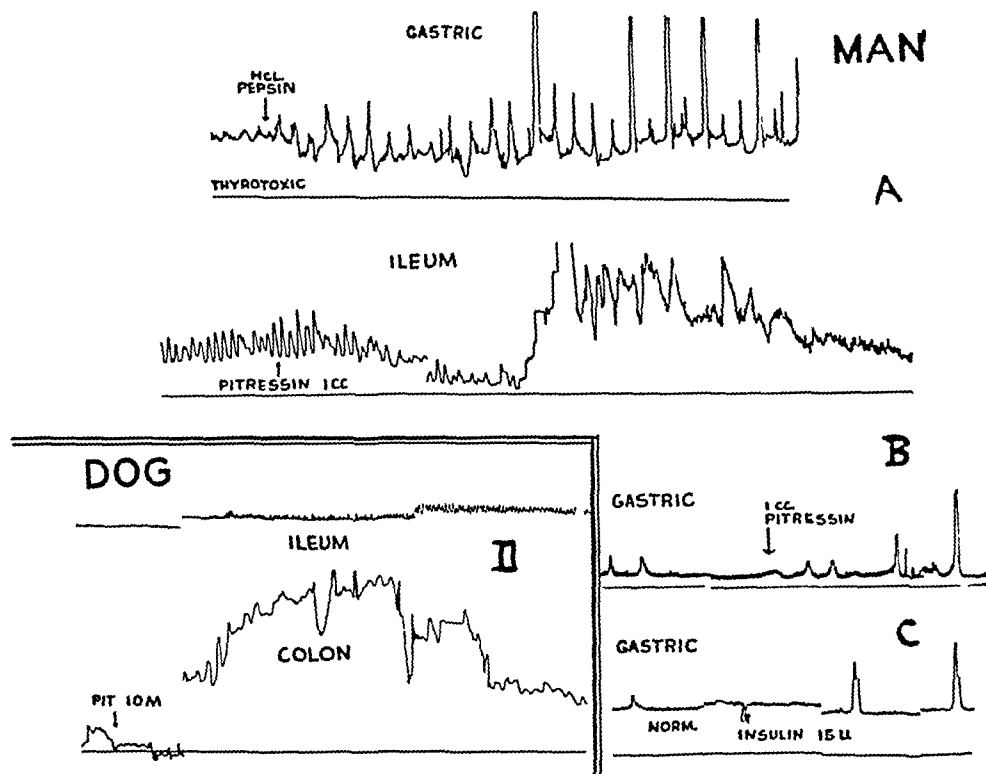


CHART 2—(A) Action of hydrochloric acid upon normal fasting human stomach. Note reduction of tone with contractions increased in frequency and greatly increased in amplitude. (B) Pitressin (1 cc) caused in the normal human ileum a preliminary reduction of tone and activity followed by greatly increased tone and peristaltic activity, particularly amplitude. In the stomach there was no change in tone but increase in the amplitude of contractions. (C) Fifteen units of insulin caused the normal fasting stomach to show contractions increased both in frequency and amplitude. (D) Action of pitressin (10 minims) in the dog caused a slight increase of tone and of frequency of rhythmic contractions of the ileum and a large increase in tone and peristaltic activity in the colon.

(b) Dog—0.65 mg subcutaneously In three animals, atropine produced no appreciable effect upon the tone and activity of the stomach and small bowel. The colon became relaxed and the activity diminished but not abolished. The effect lasted for approximately one hour.

(2) Nitroglycerine—0.65 mg (Chart 3)

(a) Man Observations carried out in two subjects showed that nitroglycerine dissolved under the tongue had transitory inhibitory actions upon both the stomach and ileum. The tone was greatly diminished and the peristaltic activity lessened in both frequency and amplitude, but not abolished. The effect lasted approximately 20 minutes. In two of the patients, hunger contractions had been induced before the administration of nitroglycerine by dilute hydrochloric acid.

(b) Dog—0.43 mg

As observed in one dog, the action of nitroglycerine upon the stomach, ileum, and colon was identical to that observed in man as described above

(3) Seconal—195 mg (Chart 3)

(b) Dog In two animals, this drug had no definite effect upon the stomach but was markedly inhibitory to the ileum and colon. Tone in both portions of the gut was markedly reduced and muscular activity of the large bowel was almost entirely abolished. Although the ileum continued to con-

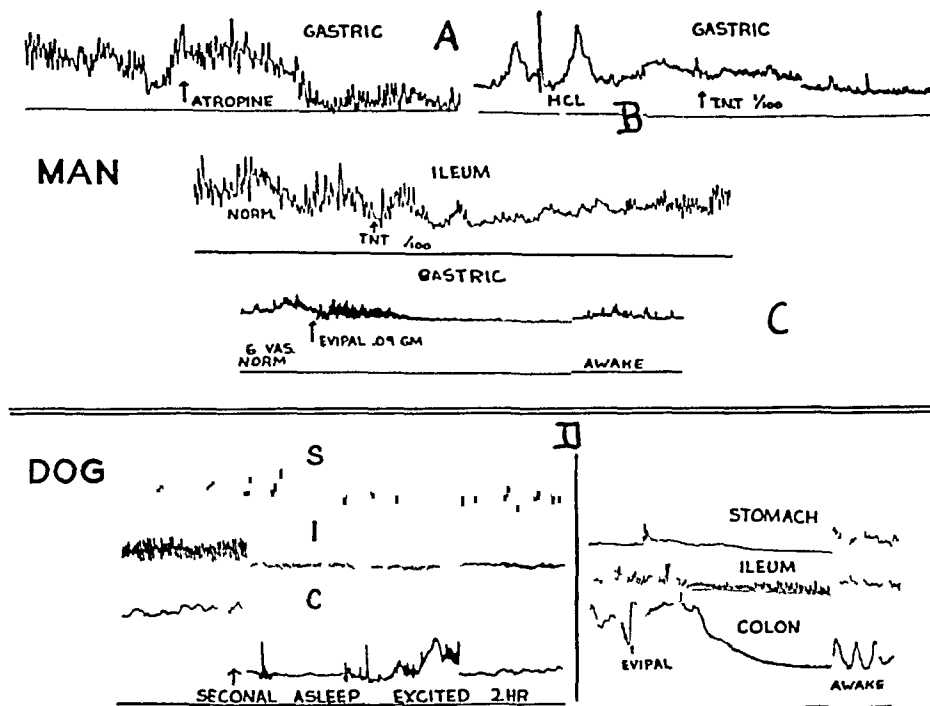


CHART 3—(A) Action of atropine (0.65 mg) upon the fasting human stomach. Note relaxation and some reduction in amplitude of contractions. (B) Action of nitroglycerine (0.65 mg) upon the human fasting stomach and ileum. Note reduction of both tone and amplitude of contractions. (C) Evipal (0.9 Gm) intravenously. Note relaxation and total inhibition of the stomach during anesthesia and prompt return of tone and activity upon regain of consciousness. (D) Action of seconal and of evipal upon the stomach, ileum and colon of the dog. Note inhibitory actions with both drugs but prompt restoration of normal tone and motility with return of consciousness after evipal, but continued inhibition two hours after administration of seconal.

tract with normal frequency, there was great reduction of amplitude. The inhibition persisted throughout the period of observation, three hours.

(4) Evipal intravenously (Chart 3)

(a) Man—0.9 Gm

In two subjects, the stomach developed an immediate reduction of tone and, with complete loss of consciousness, total abolition of motor activity. Normal tone and activity returned promptly as complete consciousness was regained (after approximately 30 minutes).

(b) Dog—0.8 Gm

In two dogs, there developed, immediately with loss of consciousness, a marked reduction of tone in the stomach, ileum and colon. Muscular activity of the stomach and colon was entirely abolished. In the ileum rhythmic contractions continued with diminished amplitude, but peristalsis was abolished.

Immediately following the return of consciousness, both tone and muscular activity became normal in all three segments of the gastro-intestinal tract

III Combined Effects (Charts 1 and 5)

(I) Morphine and Atropine

As has been demonstrated by Magnus, Plant and Miller, Orr and Carlson and Veach, morphine and atropine administered together, in therapeutic doses, counteract each other so that the motor effect of morphine and the inhibitory effect of atropine upon the gastro-intestinal tract are counteracted, and relatively little effect results

This fact was confirmed by the following observations in one man and in two dogs

(a) Man In a patient who was showing vigorous peristaltic contractions of the stomach and ileum following the administration of dilute hydro-

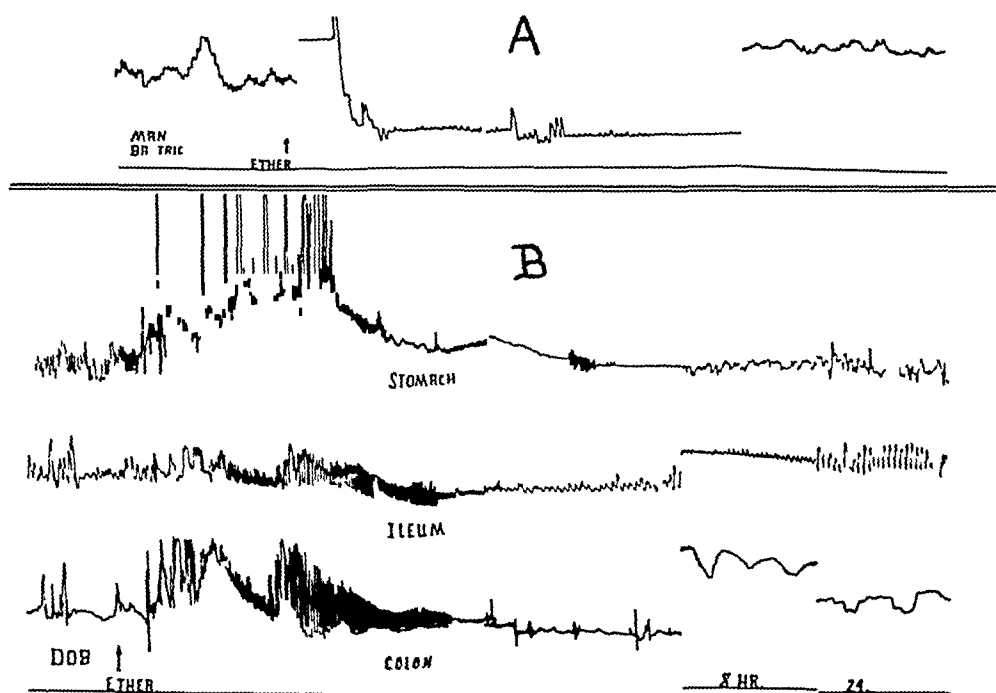


CHART 4—(A) Action of ether upon the stomach of a man and (B) upon the stomach, ileum and colon of the dog, as registered simultaneously. Note strong inhibitory and relaxing action during surgical anesthesia and restoration of fairly normal function in stomach and colon eight hours, and of ileum 24 hours later

chloric acid, atropine (0.65 mg) caused prompt abolition of activity and diminution of tone. Morphine, 16 mg, was then given and caused a prompt restoration of normal tone and activity

(b) Dog Following the retching and vomiting after the administration of 16 mg of morphine in two dogs, there was a sharp rise in the tone of both ileum and colon and a slight increase in gastric tone. In all three organs there was no change in frequency but a marked decrease in the amplitude of contractions. Atropine, 0.65 mg, given at the height of the morphine action caused the amplitude of contractions of the stomach and ileum to increase and that of the colon to decrease in one dog and had no effect in one. In the latter the tone of the bowel was diminished and that of the stomach increased

IV Anesthetic Agents

(1) Ether (Chart 4)

(a) Man The effects of ether anesthesia upon the stomach were observed in two patients and upon the ileum in one. In all three cases minor operations remote to the abdomen were carried out, namely, manipulation of a fracture in one case and vaginal plastic repairs in two. During surgical anesthesia there was a marked reduction of tone, and peristalsis was completely abolished. In the ileum, rhythmic contractions continued with diminution in both frequency and amplitude. With return of consciousness the tone and activity became reestablished slowly. At the end of 24 hours the con-

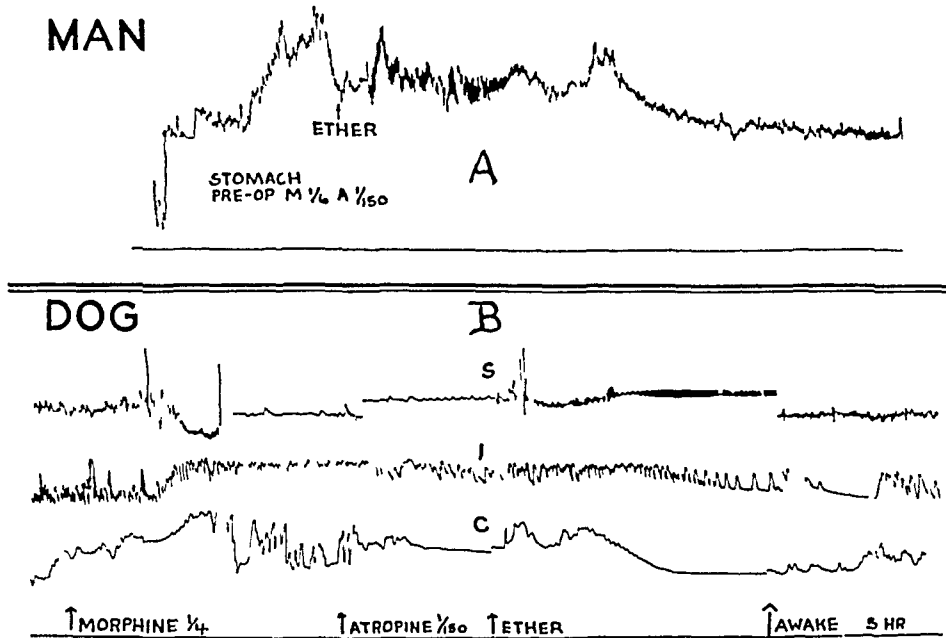


CHART 5—(A) Action of ether upon the stomach of a man and (B) upon the stomach, ileum and colon of the dog registered simultaneously. In both instances these had been administered preanesthesia medication of morphine ($\frac{1}{4}$ gr) and atropine ($\frac{1}{150}$ gr). Note that this premedication lessened the inhibiting action of ether.

tractions of the stomach were still smaller than normal. The ileum, within one hour after return of consciousness, had developed an abnormally increased degree of muscular activity.

(b) Dog Observations were made in two dogs. With induction of anesthesia there was an excitement stage characterized by rapid irregular oscillations of great amplitude and an increase in tone of both stomach and bowel. This resulted presumably from "breath-holding," vigorous contractions of the abdominal muscles and from the accompanying cyanosis. With the onset of and during surgical anesthesia there was a marked reduction of tone and cessation of motor activity except in the ileum where both rhythmic and peristaltic contractions were retained but were relatively feeble. Both tone and motor activity were slowly reestablished with return of consciousness. The colon and ileum promptly developed abnormally increased tone which was still evident 24 hours after return of consciousness. Twelve hours elapsed before the stomach had reestablished normal activity completely.

(2) Ether with Preliminary Medication of Morphine and Atropine (Chart 5)

(a) Man Premedication, morphine 16 mg, atropine 0.43 mg Records were made of the stomach in two patients, during exploration of a retroperitoneal tumor in one and during appendectomy in one. Following the irregularly increased tone and muscular activity during the excitement stage, the tone gradually lessened but throughout remained elevated above the pre-anesthetic level. Muscular activity was much diminished but never entirely abolished. In comparison with ether anesthesia alone the premedication lessened the inhibitory effect of ether.

(b) Dog Premedication, morphine 16 mg, atropine 0.43 mg Observations were made in two dogs. The effect of ether anesthesia as observed in the previous experiments became definitely altered by premedication, that is, in respect to its effect upon stomach and ileum. These organs showed no loss of tone and continued to contract feebly. The colon, however, relaxed and ceased to contract as it did under the influence of ether alone. In both stomach and bowel premedication definitely delayed the return of normal activity.

(3) Nitrous Oxide and Oxygen (Chart 6)

(a) Man The effects of nitrous oxide-oxygen anesthesia upon the stomach were studied in two cases. There occurred immediately and throughout the period of anesthesia greatly and very irregularly increased contractions. They were increased both in respect to frequency and amplitude. Tone was moderately increased. Immediately upon discontinuing the anesthesia there followed complete inhibition of motor activity and this persisted for approximately one hour. Gastric tone, however, remained slightly elevated. Motor function was reestablished slowly and was still subnormal three hours after anesthesia had been discontinued.

(b) Dog Records were made of two dogs. The stomach, ileum and colon reacted during anesthesia precisely as did the stomach of man as described above. However, after the administration of nitrous oxide had been stopped, the stomach continued to contract rapidly and violently and this was concomitant with retching. Activity in the ileum and colon was almost completely abolished and the tone diminished for 30 minutes. Normal function was reestablished in the stomach and ileum in one hour and in the colon in approximately two hours. A record made eight hours after anesthesia showed increased activity in all three organs.

The above interpretations of the records of nitrous oxide anesthesia in both man and dog are misleading. Undoubtedly the changes interpreted as increased tone and activity represented the pressure factors exerted upon the stomach and bowel by the rigidity of the abdominal muscles and by deep breathing.

(4) Nitrous Oxide-Oxygen and Ether (Chart 6)

(b) Dog In two dogs, these combined anesthetic agents produced a curious effect. The stomach responded precisely as it did to nitrous oxide-

oxygen alone in the preceding experiment. During anesthesia there was increased tone and motor activity, followed, after the return of consciousness, by decreased tone and almost total inhibition which lasted longer than two hours. The ileum and colon reacted precisely as they did to ether anesthesia alone in a preceding experiment. Tone was greatly reduced and muscular activity almost completely abolished during anesthesia but promptly became reestablished and assumed slightly exaggerated activity after consciousness was regained.

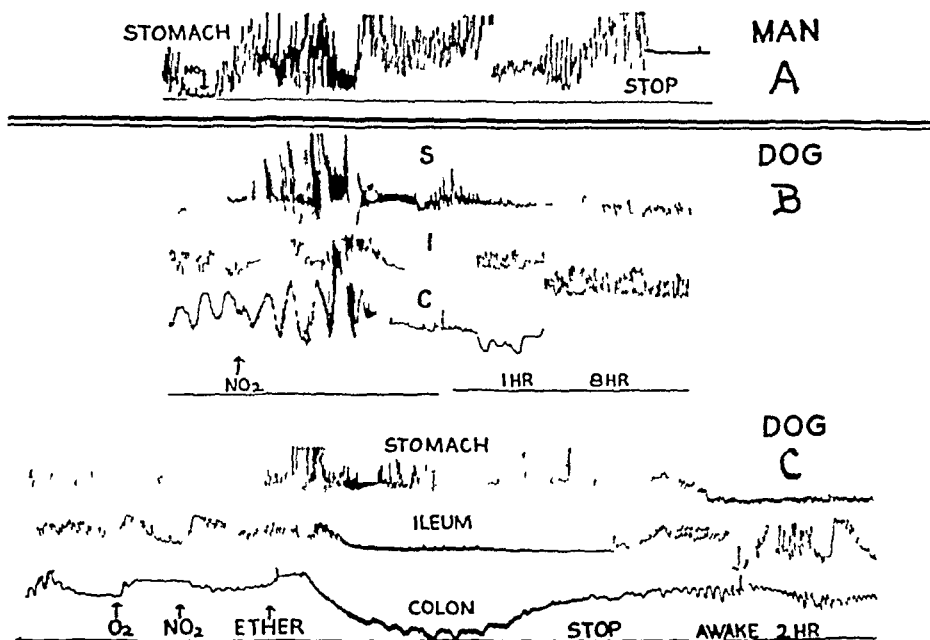


CHART 6—(A) During nitrous oxide anesthesia the stomach of a man and (B) the stomach, ileum and colon of the dog, show a primary increase of tone with irregular excursions which probably result from transmission of rapid deep respiratory excursions and the muscular rigidity associated with cyanosis. (C) Combined nitrous oxide and ether anesthesia in a dog showing inhibitory influence of ether upon the ileum and colon and the motor influence of nitrous oxide upon the stomach during anesthesia and its inhibitory influence upon this viscus after anesthesia was discontinued and consciousness was regained.

Note almost total inhibition in all organs following withdrawal of nitrous oxide and recovery from anesthesia and that the inhibition lasted for approximately one hour, and tone and motor activity were normal at eight hours.

(5) Spinal-Novocain. No premedication (Chart 7)

(a) Man. Novocain, 150 mg with ephedrine subcutaneously. Observations of the ileum and stomach were made in two patients while undergoing simple appendicectomies.

The stomach showed a slight reduction of tone and greatly diminished muscular activity during anesthesia. With return of sensation there developed normal tone and motor hyperactivity. Contractions were exaggerated both in frequency and amplitude. This state of hyperactivity persisted for at least 72 hours after operation as shown by recordings at 24, 48, and 72 hours.

The ileum developed increased tone with a slight reduction of all motor activity during anesthesia. The tone receded with return of sensation and remained relatively normal. Rhythmic contractions showed increased amplitude, and peristalsis a diminution of both frequency and amplitude.

(b) Dog Novocain, 100 mg

The influence of spinal anesthesia upon the stomach, ileum and colon was observed in two dogs. The effect upon the stomach was slightly inhibitory. Both tone and motor activity were slightly diminished. The action upon the bowel was motor. In the ileum of both dogs and the colon of one the tone and motor activity were increased. The colon of the other dog showed little or no change.

In all three portions of the gastro-intestinal tract the tone and motor activity promptly reverted to normal as anesthesia dissipated, and for three hours postanesthesia there was no appreciable change.

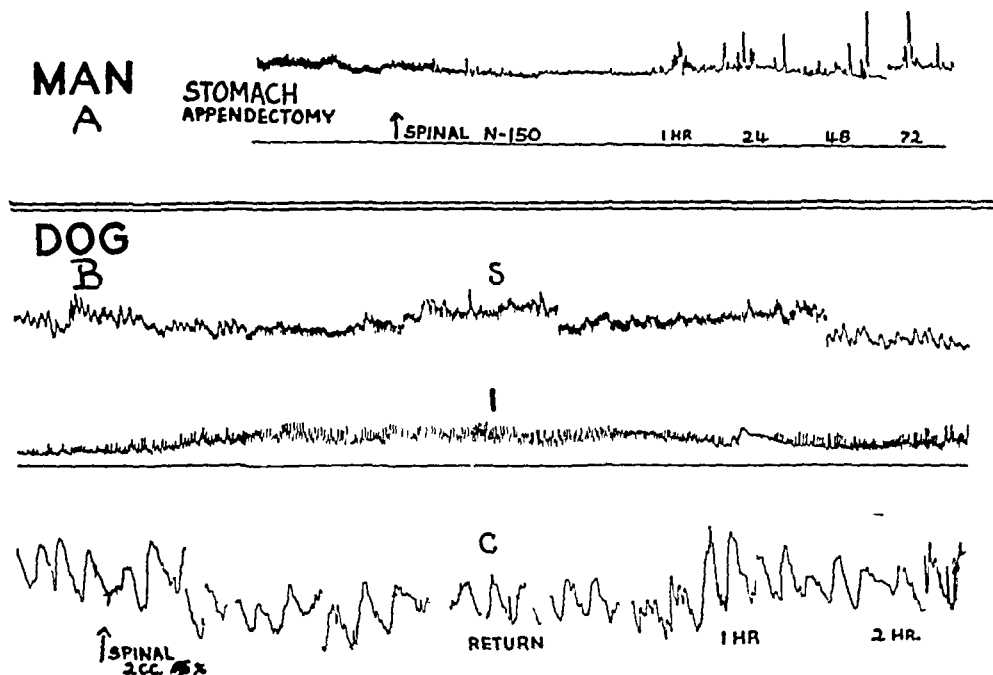


CHART 7—(A) Tracing of changes within the stomach of a man undergoing appendectomy under spinal anesthesia which reached to the level of the sixth dorsal spinal segment. Note a reduction of amplitude of contractions but no change in tone during anesthesia, and an increase in frequency and amplitude of contractions immediately following dissipation of anesthesia and at observations made 24, 48, and 72 hours later. (B) Spinal anesthesia in a dog with level of anesthesia up to the fifth dorsal segment. Note increase in tone and muscular activity of both stomach and ileum and no change in the colon, also restoration of normal tone and peristaltic activity with elimination of anesthesia and continued normal function at observations one and two hours later.

(6) Cyclopropane (Chart 8)

(a) Man. Records of the influence of cyclopropane upon the stomach were obtained in four patients, one after premedication of morphine and atropine. Two were given anesthesia without operation solely for purposes of this study. In one case, a biopsy of a cervical tumor was performed and in one a fractured forearm was manipulated. In all cases there was an increase in tone and in rhythmic contractions but inhibition of peristalsis during the stage of surgical anesthesia. Immediately upon return of consciousness there was a diminution of tone to a subnormal level and a return of normal motor activity which continued during observation periods as long as three hours.

(b) Dog. Observations in two dogs showed increased tone and activity

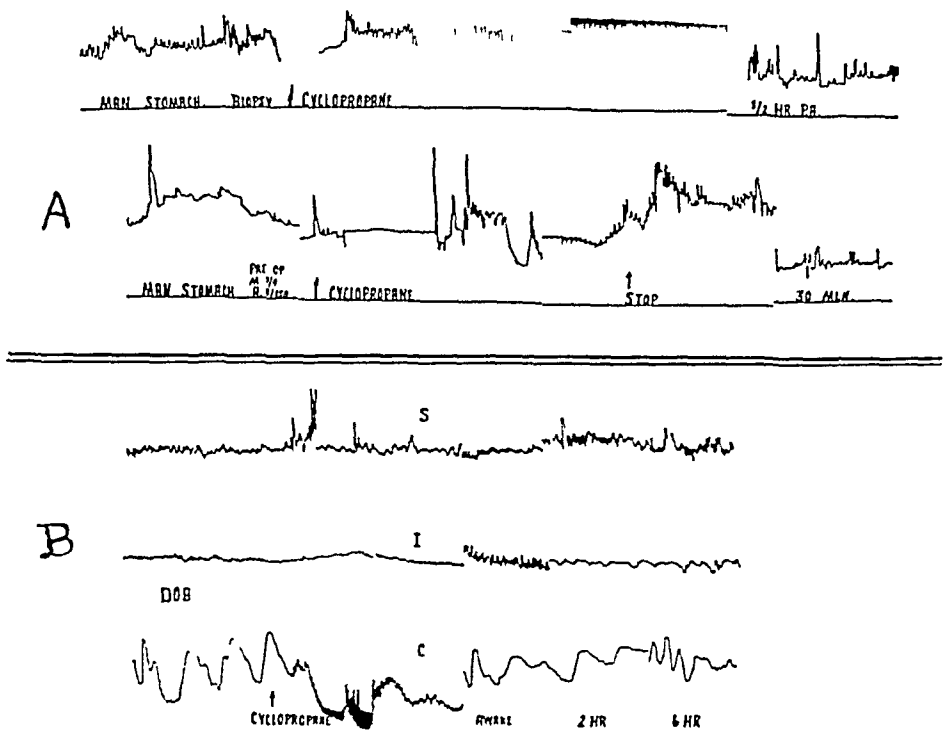


CHART 8—(A) Action of cyclopropyl anesthesia upon the human stomach first cyclopropyl alone and secondly cyclopropyl following premedication of morphine and atropine. Note that gastric tone was increased with some inhibition of contractions and that the premedication caused cyclopropyl to have less stimulating effect. (B) In the dog, cyclopropyl increased both tone and motor activity of the stomach. Increased tone of the ileum and was temporarily inhibitory to the colon. Upon a return of consciousness normal activity and tone were immediately reestablished.

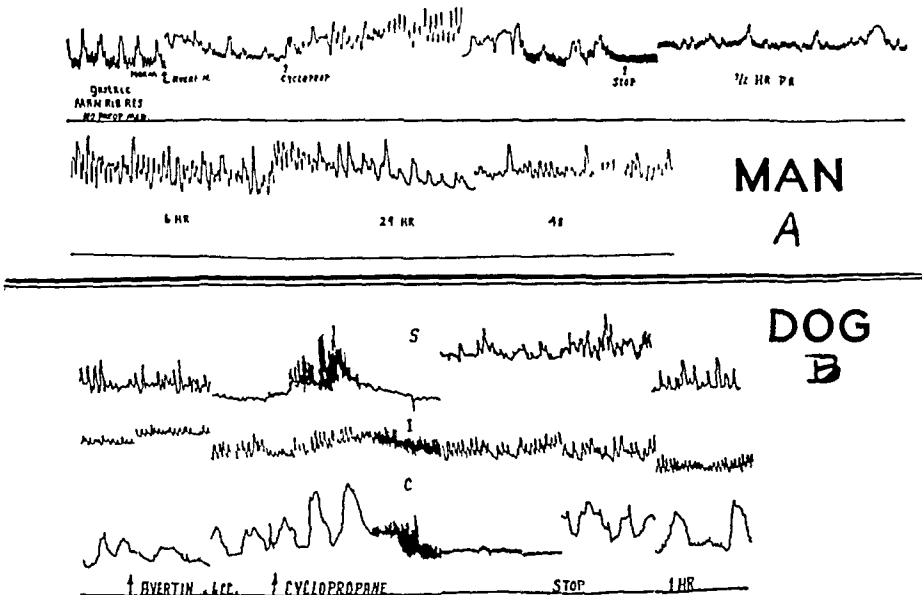


CHART 9—(A) A study of the stomach of a man made during a Schede thoracoplasty for chronic emphysema under combined avertin cyclopropyl anesthesia. Note an increase of tone with fairly normal peristaltic activity throughout period of anesthesia and restoration of normal tone and motor activity immediately following return of consciousness and hyperactivity at observations made six, 24, and 48 hours later. (B) Combined avertin cyclopropyl anesthesia in the dog caused no significant change in the stomach and ileum but was inhibitory to the colon. Normal activity in all three segments of the gastrointestinal tract returned immediately after the anesthetic was stopped and consciousness was regained.

in the stomach, increased tone and diminished activity in the ileum and decreased tone and activity in the colon during surgical anesthesia. Immediately after anesthesia was stopped the colon reestablished and retained during an observation period of six hours normal tone and activity. Aside from brief periods of abnormal activity immediately upon regaining consciousness, the stomach and ileum did likewise.

(7) Cyclopropane Supplementary to a Basal Anesthesia of Avertin (Chart 9)

(a) Man Satisfactory gastric readings were obtained in only one patient. In this patient a Schede's thoracoplasty for empyema was performed. Promptly following the rectal administration of avertin (80 mg per kg of body weight) there developed some diminution of motor activity. With the addition of cyclopropane, gastric tone and activity were temporarily increased, but with the establishment of complete surgical anesthesia the tone and activity became relatively normal. Observations made six, 24, and 48 hours after recovery from anesthesia showed a moderate degree of hyperactivity.

(b) Dog Two dogs were given 0.6 cc of avertin rectally and records made of the stomach, ileum and colon. No appreciable effect was produced. As cyclopropane was supplemented there was a brief excitement period with an increase in tone of all three segments and this was followed during surgical anesthesia by relaxation and total abolition of motor activity of the colon and by an increase in tone and motor activity of the stomach and ileum. All three segments promptly reestablished normal tone and activity with return of consciousness.

(8) Avertin, 100 mg per Kg of body weight (Chart 10)

(b) Dog Two dogs were given avertin, 0.6 cc per rectum, and observed for a period of four hours. Except for a slight decrease in tone of the ileum and colon during the period of light anesthesia, and subsequently, a moderate increase in motor activity of the stomach and ileum, no definite effect was produced.

V Oxygen and Carbon Dioxide Saturation (Chart 10)

(1) Oxygen In two dogs the inhalation of pure oxygen caused an increase in tone and an increase in the frequency of contractions of the stomach, ileum and colon but a decrease in amplitude of the contractions. Normality was promptly reestablished when administration of oxygen was discontinued.

(2) Carbon Dioxide

After a brief recovery period from oxygen administration, carbon dioxide was administered to the same animals. In both stomach and bowel there developed a reduction of tone and irregularly increased motor activity (difficult to evaluate from effect resulting from rapid, deep breathing). Immediately after removal of the mask, there was a further loss of tone in all segments and almost complete inhibition of motor activity of the ileum and colon for approximately one hour. The purpose and significance of this group of studies are dealt with in the discussion.

DISCUSSION —The drugs which were studied are representative of those commonly employed in the immediate pre- and postoperative care of patients. It has been shown that they have pronounced effects upon the tone and muscular activity of the gastro-intestinal tract. The effects of any one of them were either predominantly motor or inhibitory. However, secenal (representative of barbiturates) in therapeutic doses had mixed actions. It was motor to the stomach and inhibitory to the intestine. Also the degree with which the drugs which were studied influenced the tone and activity of the various

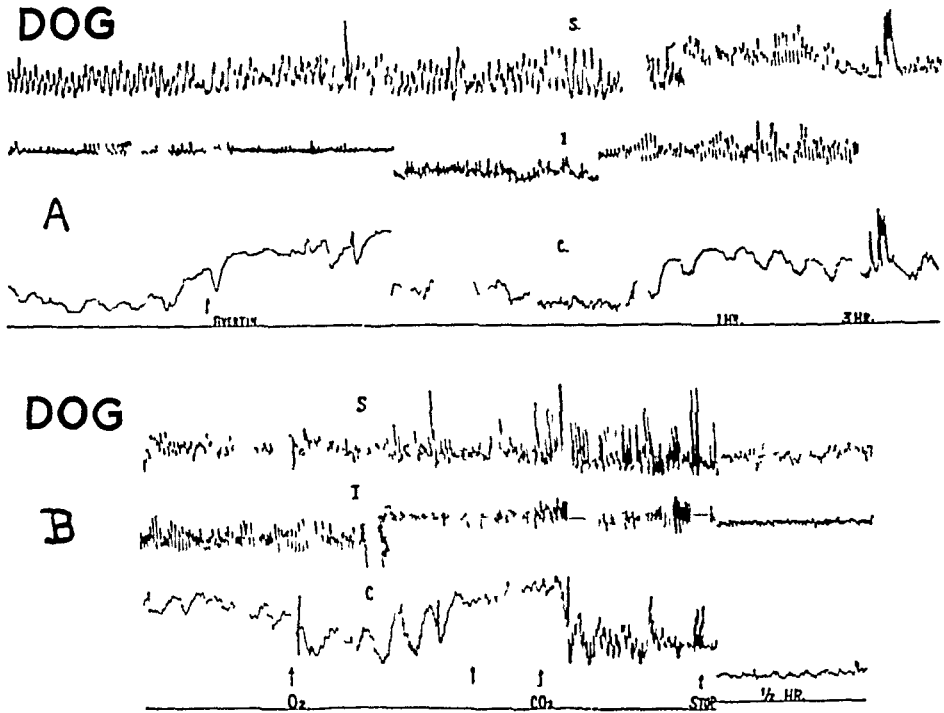


CHART 10 —(A) Simultaneous tracings of the influence of avertin upon the stomach, small intestine and colon of a dog. Note a slight motor effect upon the stomach and a slight inhibitory effect upon the colon and hyperactivity of all three organs one and three hours later. (B) Simultaneous tracings of the influence of oxygen and carbon dioxide upon the stomach, ileum and colon of a dog. In all three organs oxygen had a motor effect and carbon dioxide an inhibitory effect, the latter became more apparent after inhalations of carbon dioxide were discontinued. The inhibitory effect lasted for approximately one hour.

portions of the gastro-intestinal tract varied. As a rule the colon showed the most profound influence and the ileum the least.

In general, these experimental results are simply confirmatory of those previously reported by Schapiro, Ori, Plant and Miller, Gruber, and Robinson, Veach, Olmstedt, and Beans.

As in the case of the drugs discussed above, the anesthetic agents which were studied were either predominantly motor or inhibitory in their effects upon the gastro-intestinal tract. If tone, with or without increased activity, is used as a criterion of action, avertin, cyclopropane and spinal (novocain) anesthetics were provocative of motor responses. Ether, nitrous oxide and evipal caused relaxation of the gastro-intestinal tract with partial or complete abolition of contraction. Their actions, therefore, were unmistakably inhibitory. The true inhibitory effect of nitrous oxide became apparent only after

the anesthesia become sufficiently deep to cause some relaxation or after it was discontinued. The rigidity of the abdominal muscles, the deep breathing and the cyanosis which this anesthetic produced caused the illusion of an increase in tone and activity.

The premedication of morphine and atropine lessened the depressing effect of these inhibitory anesthetic agents.

Thus, if the reader will refer to the analysis of the clinical cases tabulated in Table I, it becomes apparent that the symptoms of disturbed gastrointestinal function occurred with much greater frequency and severity in the group of cases which were anesthetized with the depressing and inhibiting types of anesthetic agents, namely, ether and nitrous oxide, alone or in combination.

The studies of the gastro-intestinal tone and activity in both man and dog showed also that the postanesthetic reestablishment of normal tone and activity occurred more slowly in the group given inhibitory anesthetics. A period of hyperactivity developed eventually, following all anesthetics.

Curtis and his associates have shown that from 24 to 72 hours following anesthesia and celiotomy, gastric hypermotility develops and persists from two to three weeks. During the first week, the periods of increased motility were associated with epigastric distress, interpreted by the patients as gas-pains, and subsequently associated with sensations interpreted as hunger.

Why should drugs which produce anesthesia have widely different effects upon the motor activity of the gastro-intestinal tract? There is apparently no relation of such effects to their actions upon the central nervous system. Miller has shown that the effects of ether, chloroform, nitrous oxide and ethylene upon a loop of small bowel after denervation were essentially the same as they were while its nerve supply was intact.

In certain nonabdominal nonsurgical diseases there occur nausea and vomiting, distention and occasionally gas-pains. These diseases are associated with toxemia, such as occurs in pneumonia or with abnormality of either fluid or oxygen balance, such as occurs with general tissue hydration in certain cases of nephritis and with cyanosis in congenital heart disease.

With the suggestion from Dr. Roy McClure that tissue anoxia might be a factor of inhibitory influence to the musculature of the stomach and bowel studies with oxygen and carbon dioxide saturation were carried out. In each instance the inhalation of pure oxygen caused in dogs an increase in gastro-intestinal tone, and the inhalation of pure carbon dioxide caused lessening of tone and, in the bowel, almost complete inhibition of motor activity for a period of approximately one hour.

CONCLUSIONS

(1) Drugs commonly employed in the pre- and postoperative care of patients have either strong motor or strong inhibitory influences upon the tone and peristaltic activity of the gastro-intestinal tract.

(2) Anesthetic agents are in part responsible for some of the late as

well as the immediate postoperative symptoms of nausea and vomiting, distention and gas-pains

(3) The different types of anesthetics vary greatly in respect to the frequency, the degree and the duration of associated symptoms of disturbed gastric and intestinal function. Likewise, anesthetics vary greatly in their respective actions upon the gastro-intestinal tract. Cyclopropane-averitin, spinal and cyclopropane (alone) have predominantly stimulating or motor actions. Ether and nitrous oxide, either alone or in combination, have depressing or inhibiting effects upon gastric and intestinal tone and peristalsis. There is a close correlation between the degree with which gastric and intestinal motor activity is diverted from normal toward inhibition during anesthesia and the frequency, duration and severity of postoperative symptoms of gastro-intestinal dysfunction.

(4) It is suggested that the influence an individual anesthetic has upon the gastro-intestinal tract may be dependent upon its influence upon the relative quantity of oxygen in the blood or tissues during anesthesia. When inhaled, oxygen stimulates and carbon dioxide inhibits gastro-intestinal motor activity.

BIBLIOGRAPHY

- ¹ Magnus, R. Arch f d ges Physiol, 115, 316, 1906
- ² Plant, O. H., and Miller, G. H. Jour Pharm Exper Therap, 27, 361, 1926
- ³ Orr, T. G. Jour Kansas State Med Soc, 33, 3, 1932
- ⁴ Veach, H. O. Jour Pharm and Exper Therap, 61, 230, 1937
- ⁵ Schapiro, N. Arch f d ges Physiol, 41, 65, 1913
- ⁶ Gruber, C. M., and Robinson, R. O. Jour Pharm and Exper Therap, 37, 101, 1929
- ⁷ Olmstedt, J. M., and Giragossintz, G. Jour Lab and Clin Med, 16, 354, 1931
- ⁸ Beams, A. J. J A M A, 97, 907, 1931
- ⁹ Barron, L. E., Curtis, G. M., and Lauer, B. Arch Surg, 35, 675, 1937
- ¹⁰ McClure, Roy B. Personal communication
- ¹¹ Miller, G. H. Anesth and Analg, 5, 225, 1926

DISCUSSION—DR. GEORGE M. CURTIS (Columbus, Ohio) During the past five years a group of us, and particularly Louis Barron, Harry Veach, and Frank Hamilton, have become interested in this problem of gastro-intestinal tone and motor activity. Moreover, with the cooperation of a number of willing patients, we have determined the motility of the human stomach under a variety of clinical conditions, both pre- and postoperatively, as well as in certain instances under the influence of spinal anesthesia. We have observed the after-effects of operative measures under general anesthesia, although no studies have been made during such procedures.

As a consequence, we are greatly interested in this presentation, and particularly in Doctor Bisgard's excellent experimental work, in which he has demonstrated the simultaneous activity of the stomach, small and large intestines, also the effects of certain drugs as well as anesthetic agents.

Patients as a rule are not particularly averse to this procedure, and, ordinarily, cooperate well when it is explained to them. In fact, they often become interested in the graph as it develops on the kymograph. Moreover, the process of swallowing the balloon, which is deflated and enclosed in a capsule, and the subsequent intubation have their counterparts in the ordinary use of suction drainage and fractional gastric analysis.

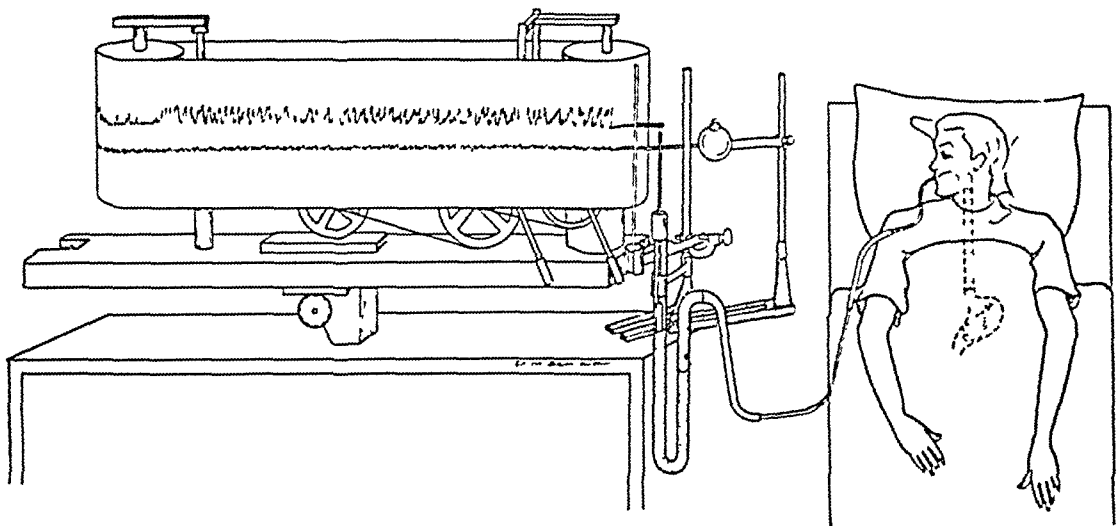


FIG 1.—The apparatus used to investigate gastric motility at the bedside (Arch Surg 32, 577, 1936)
The ink writer is described elsewhere (Jour Pharm and Exper Therap, 61, -30, 1937)

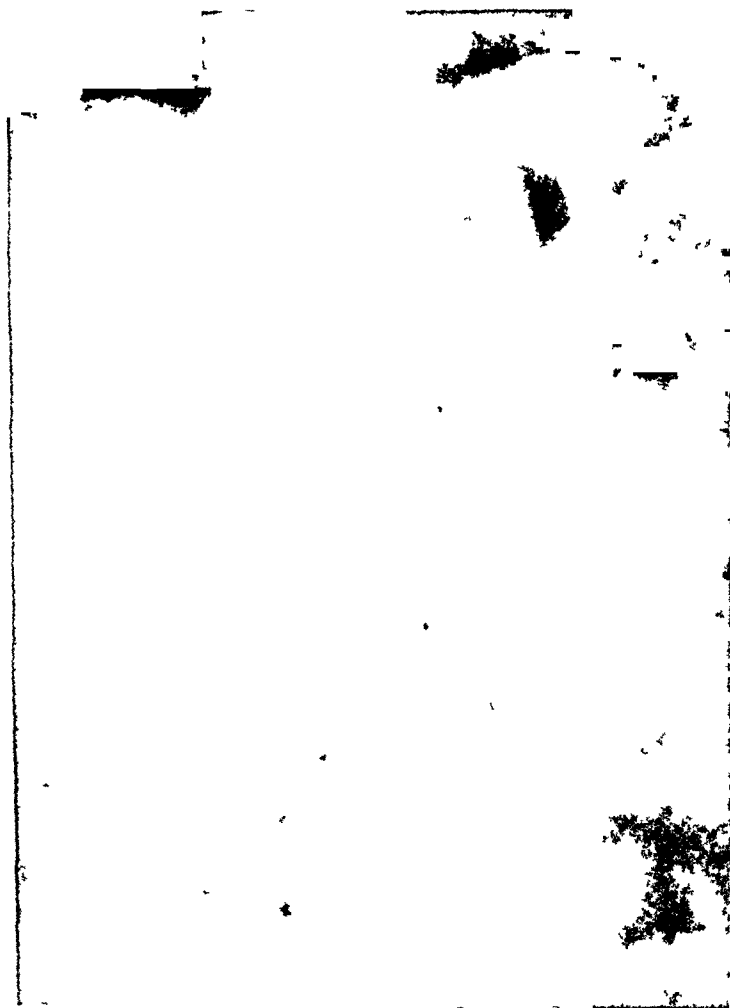


FIG 2.—The balloon in place in the stomach during motility studies (Arch Surg 32, 577, 1936)

Since the details of our extensive studies are largely a matter of record, I will allude but briefly to certain of our findings.

Figure 1 shows the apparatus which was used in making these studies. It is essentially that which Carlson used in his extensive investigations. We have added, however, one important feature. In our original studies we used the usual smoked drum, and found that the bed linen, the white interns' suits, and the nurses' uniforms were sometimes smudged by the soot. Consequently, I asked one of my residents if he would devise an ink-writer for the white paper. He was unable to do so. Later, however, there came to us, as one of our residents, a student from Starling's laboratory. Within a week, he had devised a simple ink-writer, which we now use and which makes the work in the hospital much easier.

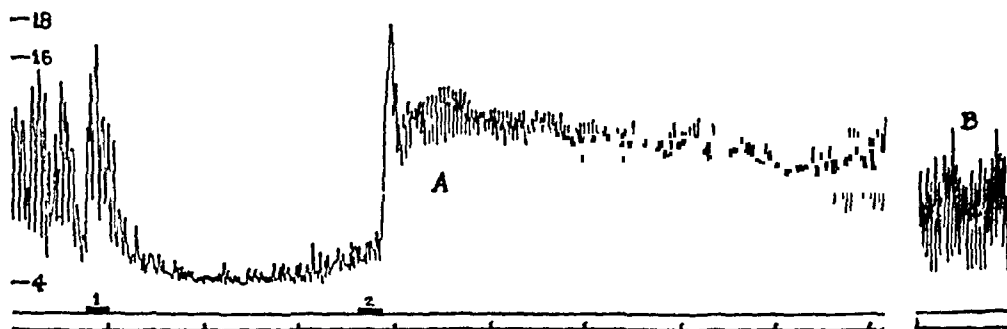


FIG 3.—The inhibitory effect of atropine (0.6 mg. intravenously) upon the motor activity of the human stomach is shown at (1). The reversal of this effect to motility by morphine (15 mg. intravenously) is shown at (2) and by (A). At (B) is shown the resultant motility after 98 minutes from (2). (*Jour. Pharm. and Exper. Therap.*, 61, 230, 1937)

Figure 2 is a roentgenogram showing the position of the balloon in the stomach. In that way it can be controlled and the tube length kept constant.

Figure 3 presents a graph showing the reversal of the morphine motor effect, as was brought out by Doctor Bisgard. Morphine was first given with an ensuing increased motility, followed by atropine given at this point with a subsequent inhibition.

From an extensive experience with this procedure we would conclude that it is readily applicable in the hospital and that it has definite clinical value in recognizing disturbances of gastro-intestinal motility and their control.

DR ALFRED BROWN (Omaha, Neb.) This excellent demonstration by Doctor Bisgard determines two points. First, gastric investigation began with the classic experiments of Beaumont made upon Alexis St. Martin. This was a case of surgical trauma and in all subsequent experiments there has been an element of doubt as to whether the results were accurate because of the trauma inflicted upon the intestine during the experiment which required the introduction of an instrument through a wound in the gut. Consequently there remained the question whether, after injury, the intestinal tract regained sufficient normality to make the readings accurate. The method of the indwelling balloon obviates the necessity for surgical trauma and we can conclude that the results by this method are accurate, because the similarity between the results on man, as shown by Doctor Bisgard, upon whom no intestinal surgery was performed, and the results in dogs, in whom the various types of intestinal pouches were made, seems to go far toward demonstrating that following surgery upon the intestine, the tract tends to restore itself to normal action.

Second, these experiments demonstrate the reasons for postoperative intestinal distention in the ether-nitrous oxide group and the lessened amount

of similar distention following the administration of cyclopropane or spinal anesthesia, which has long been recognized clinically. The ether-nitrous oxide group paralyzes the intestinal muscles. As sympathetic nerve control returns there is a resultant incoordinated action of intestinal musculature. This gives rise to irregular spasm and abnormal peristalsis causing the so-called gas-pains. Cyclopropane and spinal anesthesia act apparently on the sympathetic nervous system and there is at no time a paralysis of intestinal musculature. Consequently, postoperative return of normal peristalsis is brought about by a harmonization between the sympathetic and parasympathetic nervous systems which had temporarily been disturbed during the period of anesthesia.

The same effect is noted in paravertebral anesthesia, in which the sympathetic fibers connecting the ganglia with the somatic nerves are paralyzed. Doctor Bisgard showed a slide of a thyrotoxic patient in whom the administration of hydrochloric acid and pepsin changed an almost tonic contraction of stomach wall to normal rhythmic contraction. This same result has been noted in my cases of hyperthyroidism which have been given hydrochloric acid and pepsin during their preparation for operation. In 1930, I called attention to the diminution or absence of free hydrochloric acid in hyperthyroidism. Since that time this observation that diminished or absent free hydrochloric acid is a constant finding in hyperthyroidism has been determined in many other cases. The tonic contraction of the stomach brought about by stimulation of the sympathetic system by the hyperthyroidism accompanied by the lack of free hydrochloric acid, explains the increased appetite and accompanying loss of weight in these cases.

In some of my cases, stomach readings have also been made at the time of operation. No hydrochloric acid-pepsin was given preoperatively. The contractions of the stomach at the beginning of the operation were almost tonic, as shown in Doctor Bisgard's chart. With the administration of paravertebral anesthesia, in which the superior cervical sympathetic ganglion and nerves are temporarily paralyzed, gastric contractions changed from the tonic type to a normal peristaltic wave a few minutes after the anesthetic took effect and continued for the duration of the anesthesia.

These results raised the question as to whether the influence of anesthesia upon the sympathetic system does not also have a bearing upon postanesthetic intestinal physiology in addition to the anoxemia which Doctor Bisgard has described.

DR ROY D. McCLURE (Detroit) Doctor Bisgard mentioned the studies which we are making at the Henry Ford Hospital concerning these drugs and their relation to anoxia. He asks the question as to whether our work might show that these drugs did produce an anoxia which helps to explain his results. We have, for quite a time, been working on the question of anoxemia, and Doctor Hartman is reporting the results of that work in this afternoon's session. Unfortunately, in anesthesia as practiced to-day, we seldom have straight inhalation anesthetics, with ether, nitrous oxide or ethylene gas. In most patients, preoperative sedative drugs are given, and we have shown definitely, that the amount of oxygen in the blood is diminished after many of these sedatives as given in fairly large doses. In some instances there are direct results, in other cases, results which are more or less imperceptible by our present methods of examination. We do have evidence to show that there are varying grades of damage with resulting permanent changes in the central nervous system due to anoxia, the grade of damage being dependent upon the amount of sedatives and anesthetics. (See Anoxia. A Source of Possible

Complications in Surgical Analgesia and Anesthesia, by R D McClure, F W Hartman, J G Schnedoirf, and V Schelling ANNALS OF SURGERY, 110, 835, November, 1939)

DR PETER HEINBECKER (St Louis) I would like to ask Doctor Bisgard how many of these effects on the intestinal tract does he consider to be local effects, and to what extent does he consider them to be the end-result of an effect on the central nervous system? I think that there is little evidence to indicate that under ordinary states of anesthesia the responses to direct stimulation of peripheral or sympathetic nerve structures are affected in a paralytic way Under ordinary states of anesthesia direct stimulation of peripheral somatic and sympathetic nerve structures yields relatively normal responses

DR LEO ELOESSER (San Francisco) I should like to supplement Doctor Heinbecker's question by another I wonder whether Doctor Bisgard has made similar experiments under anesthesia during operations on the extremities? The fact that most of his operations were celiotomies has possibly added an additional complicating factor to the evaluation of the effect of drugs on the gastro-intestinal tract If these studies were made upon patients with intact, normal abdomens, this complication might be eliminated

DR J DEWEY BISGARD (closing) In answer to Doctor Heinbecker's question, Plant and Miller, at the University of Iowa, made some observations, similar to mine, of the effect of ether, chloroform and nitrous oxide, after removing the nerve supply to the isolated loop of small bowel, and they got the same responses with and without the nerve supply, so they felt that the action of these anesthetic agents was peripheral, and independent of the nervous system

In answer to Doctor Eloesser's question, several of these patients, some of those that I showed you a few minutes ago, were minor operations such as biopsies remote to the abdomen, and we got the same responses there

THE ASSAY OF GENERAL ANESTHETIC AGENTS*

HENRY K BEECHER, M D

BOSTON, MASS

FROM THE SURGICAL LABORATORIES OF THE HARVARD MEDICAL SCHOOL AT THE MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASS

PROPRIETARY anesthetic agents are appearing on the market at an increasingly rapid rate. The advocacy of first one and then another of these changes so rapidly in various institutions, a yardstick of unchanging criteria must be at hand if new agents are to be evaluated accurately and safely. If the good are to be recognized and employed and the bad discarded, a number of factors must be taken into account.

Perhaps the greatest obstacle to success in estimating the merits of anesthetic agents is our ignorance of the mechanism of anesthesia. The anesthetist confronted by the anesthesia process stands in much the same position as the internist faced with a disease of unknown etiology—his treatment must be symptomatic, empiric. The only basis we have for evaluating anesthetic agents is an empiric one. Such a method can be as logical, and successful, as the symptomatic treatment of disease often is. Just as precision and success in the treatment of disease usually considerably increase once the etiology is known, so with anesthesia. When the mechanism of the process is better understood it will undoubtedly be possible to evaluate agents with more skill than we now can. Until such progress has been made we must continue to depend upon empiric findings for our estimations.

Certainly all anesthetic agents fall short of the ideal, though some of the individual qualities of each may be nearly what we could wish. If the quality of one's evaluation is to be unchanging each agent must be pitted against the ideal, and the present discussion will be concerned with the qualities of the ideal anesthetic agent.

PHYSICAL AND CHEMICAL QUALITIES OF THE IDEAL ANESTHETIC AGENT

I *Potency, Narcotic Strength*. The most formidable enemy the anesthetist must combat is anoxia, for as Haldane has put it, anoxia "not only stops the machine but wrecks the machinery." With any agent it should be possible to use at least 15 per cent oxygen. That is to say *the narcotic strength of an anesthetic agent should be great enough so that the partial pressure† of it in the air breathed need not exceed about 650 Mm Hg.*

The partial pressure‡ required for full surgical anesthesia under several

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1930.

† The concentration of an agent necessary to produce a given level of anesthesia by inhalation may be expressed in terms of grams of anesthetic per liter of inhaled gas mixture. The anesthetic vapor or gas should not, even for deep anesthesia, occupy more than 85 per cent of the liter. Expressing it another way, it should not exert more than $0.85 \times 760 = 646$ Mm Hg partial pressure.

‡ Dry gas or vapor at a temperature of 37° C. and 760 Mm. Hg pressure.

common anesthetic agents, and the oxygen percentages permitted are detailed in Table I

TABLE I

	Partial Pressure (Mm Hg)	Oxygen Percentage
Chloroform	5	99.3
Ether	25	96.7
Ethyl chloride	35	95.4
Cyclopropane	150	80.0
Ethylene	680	10.0
Nitrous oxide	975	*

Above the line, none of the partial pressures is too high, and an excess of oxygen is possible with any of these agents

II *Solubility* When equilibrium of a gas has been established between the alveolar air and the blood, the ratio of the quantity dissolved in, say, one liter of blood to that in one liter of air is called the solubility coefficient of the gas. The solubility of an anesthetic agent in the blood must be low enough so that a relatively high partial pressure can be worked with (but not so high that the oxygen will be dangerously low), for *with a high partial pressure and a low solubility, rapid induction and rapid recovery from the anesthesia are possible*. If this test be applied to the common inhalation anesthetic agents (Table II)

TABLE II

	Partial Pressure 37° C 760 Mm Full Anesthesia	Solubility Coefficient
Chloroform	5	10
Ether	25	14
Ethyl chloride	35	2.5
Cyclopropane	150	0.49
Ethylene	680	0.74
Nitrous oxide	975	0.47

it is evident that it is successful. All those below the line have the characteristic of a rapid induction and a rapid recovery period, while those above are, by comparison, slow.

* At normal atmospheric pressure it is not possible to obtain true, deep anesthesia with nitrous oxide, even if *all* oxygen is cut out. In actual practice the patient may be depressed by means of preanesthetic medication, by basal anesthesia, and so on, to such an extent that the additive effect of nitrous oxide with 10 per cent oxygen will produce anesthesia adequate for the task at hand. Even so, in occasional cases, this is not possible without accompanying anoxia and cyanosis. Some bold individuals go so far as to use the effects of anoxia deliberately in their efforts to depress patients under nitrous oxide. Such a practice is indefensible.

III *The Hazard of Explosion* One of the great needs of surgery at the present time is an inhalation anesthetic agent that will neither burn nor explode, so that it may be employed safely in the presence of the cautery. Of the six agents we have been considering in this discussion, two will neither burn nor explode—nitrous oxide and chloroform, and yet neither of these is satisfactory, for example, for thoracic surgery nor for surgery in the mouth. Here the oxygen supply is at a premium. When the aerating power of the body is crippled, the oxygen percentage permissible with nitrous oxide is inadequate, even though only light anesthesia may be necessary. In the case of chloroform, cardiac depression of too great a degree to be allowable occurs, for these cases will be under a severe circulatory strain as a consequence of the operation, and the use of an anesthetic agent which greatly cripples the heart is not sound. This depressant characteristic makes the use of chloroform hazardous even if one is willing to ignore the possibilities of ventricular fibrillation, or of late liver and kidney damage. Aside from its well known toxic effects, the use of chloroform is hardly desirable when the cautery must be used in the air-way, for a combustion product of chloroform is phosgene, one of the deadliest of the war gases. It is highly toxic to the lungs and well known to produce pulmonary edema in even extremely great dilution.

While it is often stated that the explosive nature of ether or cyclopropane or ethylene with oxygen is of comparable degree, data recently gathered tend to throw doubt on this. Possibly static electrical charges have a greater tendency to detonate ethylene-oxygen, or cyclopropane-oxygen mixtures than is true for ether-oxygen. However that may be, the fact remains, *with the ideal agent, explosive mixtures will not be formed with air or oxygen*.

BIOLOGIC QUALITIES OF THE IDEAL ANESTHETIC AGENT

I *A Controllable Route of Administration Must Be Available* At the present time, the most controllable route for the administration of general anesthetic agents is by inhalation. A recent trend makes the consideration of nonvolatile agents of importance. There are two main routes of administration of nonvolatile agents for general anesthesia—the veins or the rectum. Some agents, as avertin, can be introduced only through the rectum. But in the case of the barbiturates, many can be introduced directly into the blood stream. The recent recommendations of a half-dozen papers, that the barbiturates be introduced rectally, raise the question of the relative controllability of these two routes of administration.

Several points are pertinent to such a consideration.

(1) *Once an agent is placed in the rectum it is nearly impossible to recover any* after it begins to exert its normal action or to give toxic effects. While high colonic enemas may be tried, in an endeavor to wash it out, the fact is, such action may sweep the offending agent higher in the bowel and allow even more rapid absorption with greater toxic effects to follow.

(2) Even though a solution of given volume may be injected into the rectum at a standard speed, *it is impossible to say to what height it will travel up the bowel*. There are a number of reasons for this. There is no need to point

out to a group of surgeons how uncertain cleansing of the bowel may be as a result of routine enemas. The height to which an anesthetic agent will rise on being placed in the rectum is determined in large part by the fecal content of the bowel. Other factors active in regulating height (and impossible of accurate evaluation) are tone of the bowel, peristalsis, and anatomic anomalies. Using a dilute barium solution under exactly the same conditions as avertin is used, Sebenius² found on roentgenographic examination that in two patients the entire colon including the cecum was filled, in two the midascending colon was reached, while in four the hepatic flexure was attained and in four the midtransverse colon, in seven the splenic flexure and in one patient only the rectosigmoid junction was reached.

(3) It is well known that *the toxicity of the nonvolatile anesthetic agents depends to a great degree upon their rate of absorption*. With some of the agents, as with sodium barbital, while the blood level is rising as a result of absorption, it is counterbalanced by excretion through the kidney and a safe blood level may thus be maintained. In other cases, as with the fast acting barbiturate, evipal, a safe blood level depends in part upon liver destruction concomitant with absorption. An abnormally rapid rise in the absorption rate, however, easily upsets the balance experience has taught is safe, and serious toxic effects follow.

(4) The following statement, then, seems to be a reasonable one. If we cannot efficiently remove an agent once it is placed in the rectum, if we cannot control the height to which a solution injected into the bowel will rise, then it follows that we cannot control the rate of absorption. In other words, we cannot accurately control the toxicity of nonvolatile agents used rectally. If an agent can be used intravenously there is no reason to resort to the relatively inaccurate and unsafe rectal route. I wonder if the defenders of the rectal route of administration of the barbiturates are prepared to claim that there is any magic in the *route* of absorption. The implication is inescapable in some of the papers referred to, that rectal administration prolongs the action of the drug¹. The rate of administration can be precisely controlled through intravenous drip methods, and if toxic signs appear, the administration can be immediately curtailed. It seems evident that such a method is more desirable than one which cannot be precisely controlled.

II *Factor of Safety, Toxicity*. The anesthesia process is by definition a reversible depression. It is a reversible approach toward death. This possibility of accident ought always to be remote. If any anesthetic agent allows irreversible change to occur, allows death to come near without adequate warnings far in advance and before irreversible change has occurred, it cannot be considered satisfactory. The well worn examples of ether and chloroform illustrate this. With ether over-dosage, the respiration fails and intake of the drug stops long before serious damage has occurred. Under chloroform, subtle and irreversible changes of fatal degree may occur in the liver and kidneys with no warning to the anesthetist. Or ventricular fibrillation may strike without warning. It is not yet possible to say whether or not such a

potentiality may greatly curtail the usefulness of cyclopropane, there is, however, worrisome evidence that this may be the case. To sum this up *No side-toxicity other than that inherent in the anesthesia process itself should be present*, and easily detectable phenomena should warn of approaching danger long before the patient has suffered from the toxic effects of the drug used.

III Adequacy of Physiologic Effect Surgery of precision should be permitted without hurry or hindrance. In any such requirement, effects that are too widespread may also be a problem. With inhalation anesthesia the wasteful crippling of many of the organs of the body when anesthesia of only a limited region is desired, is unpleasant to contemplate. Observations of the last few years suggest that even inhalation anesthesia may increase in its specificity.

A great stumbling block to progress in knowledge of the anesthetic agents has been their multiple actions. There is the general action producing loss of consciousness, and specific actions attacking one system but not another. If we did not have proof that these dual effects could be turned to practical advantage, it would seem fanciful to suggest that such might be the case. But it is the case.

In the laboratory, we have learned that chloralose produces general anesthesia but spares the carotid sinus mechanism, that certain of the barbiturates spare the sympathetic nervous system. Clinically, we know that cyclopropane disturbs fewer organs than ether. If this agent is found in time to meet the requirements of usefulness and general safety outlined above, it must be accepted as a step forward. Extraordinary is the clinical finding that *sub-general anesthesia* doses of trichlorethylene will produce anesthesia of the fifth cranial nerve. A further requirement of the ideal anesthetic agent can be stated: *The normal activity of only a few organs shall be impaired*.

IV Elimination The ideal anesthetic agent will be one which is either rapidly destroyed or swiftly eliminated even in the presence of grave organic disease. One reason for the superiority of inhalation anesthetic agents over those of the nonvolatile group for general anesthesia lies in the ease of control of the volatile agents, and of most importance is the speed at which they can be eliminated if toxic effects appear. Progress in developing nonvolatile compounds that are rapidly eliminated through the kidneys or are rapidly destroyed by the liver, as in the case of the fast acting barbiturates evipal, pentothal, and others, raises the possibility that similar agents may be found, in time, to fulfill the requirement of controllability better than a gas or a vapor. Such is not yet the case. With the nonvolatile agents there is the further complicating factor that individual susceptibility varies widely. This has been illustrated many times both for barbiturates and for avertin.^{1,3}

STATISTICAL REQUIREMENTS

The inescapable test to which most innovations in medicine must be subjected is whether or not they can lower the death rate for a given procedure.

Statisticians and their statistics are looked upon with considerable suspicion by the rest of the world. Statistics are not a substitute for common sense. On the other hand, some use of statistical methods is essential if common sense is to be preserved in the handling of data.

Anesthesia literature, perhaps more than that of any other division of medicine, is shot through with claims wholly unsupported by available evidence. No one can object if an individual wishes to report a few hundred anesthetics with no deaths. In certain cases, such reports are desirable, as, for example, when a new anesthetic agent is being tried and no one man has had opportunity to acquire a really adequate personal series. Strenuous objections can be raised and should be, if such reports contain any attempt to draw conclusions as to the safety or death rate or to make comparison with other agents of a similar or lower death rate.

Whether we like it or not, the fact remains that if anesthetic agent A has a death rate of 1/1000 cases we need data of the order of 10,000 cases with about ten* deaths before we can make any statements as to the death rate of that agent.

If the death rate of anesthetic agent B is 1/10,000 cases we need the order of 100,000 cases with, again, about ten instances of death attributable to the agent, in order to make any statement as to the death rate of that agent.

It is sometimes said that the death rate directly attributable to ether anesthesia is 1/10,000. In order to prove that another agent is better than ether in this respect, we must have, then, not less than about 100,000 cases of the other agent, under comparable conditions, if we are to *prove* that the other agent excels or even equals ether as far as death rate is concerned.

Stating the foregoing in general terms, we must deal with so many cases that the square root of the number of deaths is not greater than about one-third of the number of deaths †.

More attention to these points would cut down on the frequency with which institutions advocate a given anesthetic agent or a given procedure only to have abandoned that procedure or that agent by the time the report concerning it gets into print.

CONCLUSIONS

New drugs for general anesthesia must be tested by constant criteria if they are to be compared with established agents. The irreducible minimum of simple, arbitrary requirements of the ideal general anesthetic agent is described. Important from the point of view of physical and chemical qualities are Potency or narcotic strength, solubility in air and blood, and explosibility. From the more strictly biologic aspect of the question, the elements of importance are Controllability of the route of administration, side-effects and toxicity of action, adequacy of physiologic effects for the

* It might be argued that six deaths are adequate, however, for a conservative estimate ten are safer.

† I am indebted to Professor E. B. Wilson for advice here.

task at hand, specificity of action, elimination. Statistical requirements are considered in relation to the mass of data necessary to permit dogmatic statements to be made as to death rate and general safety. The use of these criteria is illustrated by testing the common anesthetic agents.

REFERENCES

- ¹ Beecher, H. K. Fatal Toxic Reactions Associated With Tribromethanol (Avertin) Anesthesia. *J A M A*, **111**, 122, 1938.
- ² Sebening, W. Recent Researches and Clinical Advances in Avertin Narcosis. *Anesth and Analg*, **11**, 145, 1932.
- ³ Weiss, S. The Therapeutic Indications and the Dangers of the Intravenous Administration of—(Various)—Barbituric Acid Derivatives. *Am J Med Sc, N S* **178**, 391, 1929.

TRENDS IN INHALATION ANESTHESIA^{*}

WESLEY BOURNE, M D

MONTREAL, CANADA

THE TRANSCENDENT PRINCIPLE of reversibility in anesthetic action, wherein perception by the senses may be suspended and restored, constitutes a boon to man, and since the universal adoption of inhalation anesthesia nearly 100 years ago, the scope of laboratory investigation has increased and the aim of surgery in humane rescue extended.

It was not long, however, before the ill effects which anesthetics are capable of producing became apparent, indeed, as early as January, 1849, in Magdeburg, Dollhoff¹ observed delayed chloroform poisoning. The ravages of this drug are so well known that it might be numbered among Erasmus' *inverse Silem of Alcibiades*. Any time these hundred years, an important trend has been to disclose completely the influences of anesthetics on vital processes, and numerous data exist concerning the effect of anesthetics upon metabolism, as represented by blood findings, liver changes and the composition of the urine. The facts have been recounted elsewhere^{2, 3} and it is not practical, at this time, to do more than generalize discursively.

With regard to the effects of inhalation anesthesia on the blood, two of them have clinical significance, namely, concentration and acidosis. Chloroform and ether cause marked blood concentration, which is due chiefly to the migration of water from the blood to the tissues. This blood concentration is adequately lessened by the administration of water or dilute solutions, and everybody knows how readily these are absorbed in proportion to the depth and duration of the narcosis. By analogy, it would seem that the degree of concentration is not nearly so great with the gases, nitrous oxide, ethylene and cyclopropane, at least there is nothing like the same avidity for fluids. The tendency of late, therefore, is to employ the gases more and more and especially in the case of the dehydrated patient. It may be mentioned, that from the falling-drop fundamental of Barbour and Hamilton,^{4, 5} "the advent of a method by which blood and plasma specific gravity changes can be followed from minute to minute, with single drops, opens a field of application to very acute shifts in the water balance, such as occur, for instance, in anesthetic and operative shock. One can also evaluate procedures designed to combat these conditions, such as the administration of morphine or alkalis. The method further permits following the administration of fluids in various acute toxemias. While fluids are actually being given, the blood condition can serve as a guide to the therapeutic procedure. Anesthetic shock, as the trend of recent investigation shows, is closely bound up with acidosis and anhydremia. It is possible that in this instance the water content of the blood is

^{*} Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

of equal if not greater importance than blood pressure" Determinations along these lines are now being made at the Presbyterian Hospital, New York City,⁶ and in Montreal, by O'Shaughnessy and myself at St Mary's Hospital It is hoped soon to obtain some valuable information

It has been shown that the acidosis of anesthesia is a true acidosis, that is, the alkali reserve is lowered and the hydrogen ion concentration is increased, that phosphoric and lactic acids are discharged from the muscles, in part held in the liver until the resumption of kidney function after recovery, and then in some measure redistributed as well as excreted It has been shown, too, that this acidosis may be lessened by building up the glycogen reserves of the body before a surgical operation, and that the acidosis of anesthesia may be reduced considerably by the rectal administration of copious quantities of a specially balanced hypotonic alkaline sodium and potassium phosphate solution immediately after operation This bulky, watery, and alkaline solution not only obviates the acidosis, but decreases the blood concentration, and also ameliorates the patient's condition during recovery by virtue of its potassium ions, said to be the most stimulating of all to any depressed living thing, especially when the phosphate anion is present and when the medium is alkaline Although I disapprove the use of glucose solutions during operation for the simple reason that at this time hyperglycemia is apt to be present, I commend their employment before operation and after complete recovery from anesthesia A trend in inhalation anesthesia is to allow fluids to be diffused more freely Let us liken them to the healing waters of the Onchestus described by Aristotle

In olden times the liver was thought to be the seat of love or lust and in this manner the father of Euphuism, the Oxonian, John Lyly, of Elizabethan days, made mention of it in his *Endymion* as "It tickleth not my liver" Whether or no it be true that such passion saps vitality, we must now behold the liver with other than amatory eye The liver is a prodigious organ, possessed of multiform activities, assimilatory and secretory, diurnal and rhythmical⁷ However, despite its magnitude and physiologic importance, its cells are exceedingly susceptible to injury, so that in the very performance of their duties they are apt easily to succumb But their regenerative powers are remarkable As long ago as when the Pasteur Institute was founded (1886), Bizzozero⁸ and von Podwyssozki,⁹ separately, showed that loss of liver substance is replaced by proliferation of the liver cells and the cells of the small bile ducts Confirmation and amplification have been given to this by several other observers, and Mann and Magath¹⁰ demonstrated that about 70 per cent of the dog's liver may be removed without serious damage to the portal and vena cava circulation In a few months the remainder will be enlarged and the amount of tissue practically the same as before operation What a prolific regeneration! The Ancients must have had some conception of this when they told of Prometheus chained on Mount Caucasus and subjected to the daily attack of an eagle (probably a vulture) which, for ages, preyed upon his liver, yet succeeded not in consuming it Let us say with

Carlyle, that the minds that made such stories are here yet How strangely things grow, and die, and do not die! It is well that there is such an excess of liver tissue and that its cells are so readily capable of karyokinetic multiplication, but in the instance of poisoning, as from chloroform or phosphorus notwithstanding liver regeneration and the normal appearance of the tissue under the microscope, it has been proved, since the introduction of the dye tests, that complete functional recovery is not fully established for some considerable time later A trend has been, therefore, to compare the effects of anesthetics on the liver by employing the biomsulfalein detoxification test Suffice it to say that chloroform is maximally damaging to the liver, ethyl ether and vinyl ether slightly so, and the gases, nitrous oxide, ethylene and cyclopropane, in themselves, not in the least harmful But when there is not an adequate supply of oxygen during the anesthetics of chloroform and the ethers, the liver function impairment is markedly enhanced, and in the instances of the gases, nitrous oxide and ethylene, there will be considerable injury Such does not prevail in cyclopropane anesthesia as a superabundance of oxygen is always given From a consideration of the effects of anesthetics on the liver, we learn to eschew chloroform and to avoid anoxia At this juncture, it is apposite to draw attention to the destructive change in the brain when asphyxia accompanies nitrous oxide anesthesia, so explicitly described by Courville^{11, 12}

The changes which anesthetics may produce in the kidney seem to be analogous to, and concurrent with, those in the liver It has been known for a long time that anesthesia, generally, diminishes the volume of the urine secreted From various observations, it may be said that all inhalation anesthetics cause some depression of kidney activity, whereby the rate of secretion and composition of the urine is lowered, that the degree of depression varies directly with the depth of narcosis, and that the effects are influenced by the condition of the kidneys, by the water content of the blood, and by the duration of the anesthesia Even during cyclopropane anesthesia, Waters and Schmidt¹³ have shown that the urinary output is usually suppressed and a compensatory increase occurs several hours following

From these desultory remarks concerning the interferences with metabolism which anesthetics may bring about, it can be seen that the trend has been to employ less toxic drugs, to use combinations of them, to improve the methods of their administration, and to offset and alleviate their deleterious actions, for by how much the more these *principia* are observed, by so much the more will surgery be endured Thus it was that ethylene and cyclopropane, in their times, were brought forward, thus it is that Lundy¹⁴ has stressed the principle of combining regional and general anesthetics, and quite recently¹⁵ recommends pentothal sodium intravenously for inducing anesthesia, especially in hypersensitive individuals, to decrease the stages of excitement and avoid cyanosis, particularly in cases of high blood pressure—this is an excellent procedure, and I am pleased to have followed it, thus it is that intratracheal methods were developed to prevent obstructions to breathing

and to produce quiet respiration, thus, too, it is that the use of fluids has increased and oxygen is given so freely

While we must be very careful continually to remember the beneficial actions of inhalation anesthetics, we cannot but admit their limitations, and comprehensively the trend is to select those anesthetic agents and methods of administration that are least harmful. In the light of our present knowledge, it would seem rational to choose one of three procedures—namely, regional anesthesia, that is, “local,” on one of the various forms of “block” anesthesia, or “spinal”, or general anesthesia with nitrous oxide or cyclopropane, or a combination of the two. All other forms of anesthesia seem doomed soon to desuetude, at least in major surgery. I admit at once that the advantages of spinal anesthesia are very great, particularly on account of the muscular relaxation and the excellent recovery, particularly, too, for surgery of the upper abdomen and in thoracic surgery. Perhaps the devotees of inhalation anesthesia are inclined to regard this as an adverse trend.

The all-pervading desire for improvement and the increasing demands of surgery continually give tendency to change in anesthesia, and cynosures in this regard, of late, are the employment of cyclopropane, the absorption of carbon dioxide, and the administration of anesthetics by the closed intratracheal technic. The advantages of cyclopropane are already too well known for me to be prolix in the matter, but it may be said that a splendid combination is avertin per rectum, to the patient in bed, half an hour before operation, followed in the operating room by a mixture of cyclopropane, nitrogen and oxygen. The removal of carbon dioxide from the expired air permits the continued and repeated use of anesthetic materials. The closed intratracheal method precludes respiratory obstruction, obviates interference with some surgical procedures, gives absolute assurance of a plentiful supply of oxygen directly to the lungs, affords quieter breathing and a softer abdomen, although narcosis is not profound, and supplies the ready application of Guedel's method of artificial control of respiration. Observing all due precaution against making arbitrary arguments, one might go on to relate other examples. Even a casual review of recent literature suggests, here and there, the influence of these centers of attraction, direct or indirect, upon the practice of inhalation anesthesia.

In the general course which inhalation anesthesia is taking, one notices the increasing attention paid to the preparation of the patient for operation. We cannot be too careful in this direction, indeed, we are still too much inclined to neglect some of the important considerations and to hasten the matter. One thing that I do feel we should be more particular about is the problem of fear, so shamefully disregarded, especially in larger institutions. Fear may lead to phantasmagoria of excruciating incident to the patient going under an anesthetic, something like the wild ideas in the land of dreams depicted by Edgar Allan Poe in some of his weird but beautifully written tales of mystery and imagination. This source of terror may lead to severe shock, or at least to a tremendous dissipation of nervous energy. Remember the

almost prophetic words of Oliver Wendell Holmes, that "it is better to lose a pint of blood from your veins than to have a nerve tapped. Nobody measures your nervous force as it runs away, nor bandages your brain and marrow after the operation." How aptly this thought implies that we ought to do all in our power to assuage fear in one to whom an operation is proposed, by the cultivation of a psychologic approach intended to inspire confidence, gain reliance, and induce harmonious contentment. In fine, the anesthetist does well to take upon himself the rôle of *μουσικός*, that is, as Plato meant it in the broader sense.

REFERENCES

- ¹ Casper's Wochenschrift, 1, 58, 1850
- ² Bourne, Wesley. Anaesthetics and Liver Function. *Am J Surg*, 34, 486-495, 1936
- ³ Bourne, Wesley. Factors Determining Selection and Administration of Anaesthetics. *Surg, Gynec and Obstet*, 68, 519-526, 1939
- ⁴ Barbour, H. G., and Hamilton, W. F. The Falling-Drop Method for Determining Specific Gravity. *J Biol Chem*, 69, 625-640, 1926
- ⁵ Barbour, H. G., and Hamilton, W. F. The Falling-Drop Method for Determining Specific Gravity. *J A M A*, 88, 91-94, 1927
- ⁶ Scudder, J., Zwemer, R. L., and Whipple, A. O. Acute Intestinal Obstruction. Evaluation of Results in Twenty-one Hundred Fifty Cases, With Detailed Studies of Twenty-five Showing Potassium as a Toxic Factor. *ANNALS OF SURGERY*, 107, 161-197, 1938
- ⁷ Forsgren, E. Über die Rhythmik der Leberfunktion und des inneren Stoffwechsels. *Acta Med Scandinav Suppl*, 59, 95-96, 1934
- ⁸ Bizzozero, G. Über die Regeneration des Elements der Gewebe unter pathologischen Bedingungen. *Centralbl f d med Wissensch*, No 5, 1886
- ⁹ Podwysozki, W. von, Jr. Experimentelle Untersuchungen über die Regeneration des Lebergewebes. *Beitr z path Anat u z allg Physiol*, 1, 259-360, 1886
- ¹⁰ Mann, F. C., and Magath, T. B. The Production of Chronic Liver Insufficiency. *Am J Physiol*, 59, 485, 1922
- ¹¹ Courville, C. B. Asphyxia as a Consequence of Nitrous Oxide Anaesthesia. *Medicine*, 15, 129-245, 1936
- ¹² Courville, C. B. Pathogenesis of Necrosis of the Cerebral Gray Matter Following Nitrous Oxide Anaesthesia. *ANNALS OF SURGERY*, 107, 371-379, 1938
- ¹³ Waters, R. M., and Schmidt, E. R. Cyclopropane Anaesthesia. *J A M A*, 103, 975-983, 1934
- ¹⁴ Lundy, J. S. Recent Advances in Anaesthesia. *J A M A*, 110, 434-436, 1938
- ¹⁵ Lundy, J. S. Personal communication

ANOXIA*

A SOURCE OF POSSIBLE COMPLICATIONS IN SURGICAL ANESTHESIA

ROY D McCLURE, M D, F W HARTMAN, M D,
J G SCHNEDORF, M D, AND VICTOR SCHELLING, Ph D

DETROIT, MICH

FROM THE DEPARTMENT OF SURGERY AND THE DEPARTMENT OF LABORATORIES, HENRY FORD HOSPITAL, DETROIT, MICH

THE RECENT WORK of Couville¹ on "Asphyxia as a Consequence of Nitrous Oxide Anesthesia," and the pathogenesis of the cerebral narcosis resulting from the same have served to concentrate interest and increase knowledge of the whole field of asphyxia or anoxia in which the physiologists, led by Yandell Henderson,² Barcroft,³ and others, have been pioneering for years. The anesthesiologists Schmidt,⁴ Shaw, Steele and Lamb,⁵ Seever and Waters,⁶ Raginsky and Bourne⁷ and others have probably followed the physiologists most closely as evidenced by their more recent contributions. On the other hand, the pathologists have been slow to interest themselves and correspondingly less helpful in the recognition of the gross and microscopic lesions despite the admonition of Henderson that "asphyxia is the most frequent and most important of all pathologic processes. A large part of all the structural abnormalities that the pathologist studies involve perversions of tissue respiration."

Couville⁸ sums up his observations as follows: "As a rule these patients developed respiratory or cardiorespiratory failure while under nitrous oxide-oxygen anesthesia and failed to regain consciousness when the anesthetic was withdrawn. During the survival period the patients remained in coma, frequently had convulsions and most of them died in a state of hyperthermia after an interval of 1½ to 26 days. A few individuals recovered, some with a residual lenticular syndrome, others with a permanent psychosis, while some fortunately recovered completely. In the fatal cases the cerebral cortex and the lenticular nuclei presented areas of necrosis which at times became confluent and if a survival period was sufficiently long, resulted in astrovacular scars." Thus a classical picture of anoxia is drawn which may apply equally well to the condition produced by the various narcotics and anesthetics, or their combinations.

Oxygen want occurring with nitrous oxide anesthesia (Brown, Easson, Lucas and Henderson⁹) is readily appreciated because it is necessary to administer 80 per cent to 95 per cent concentration of this gas to get good anesthesia, thus reducing the arterial oxygen tension directly at first and later by depression of the respiratory center, producing anoxic anoxia. The other types of anoxia—*anemic*, due to lack of, or inactivation of, hemoglobin, *decreasing its capacity to take up oxygen*, *stagnant*, due to retardation of the

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

circulation and transportation of oxygen, and histotoxic, due to drugging of the tissue cells so that they cannot utilize the available oxygen—are to be kept clearly in mind. As this study will demonstrate, it is usually a combination of all or several of the types which results in serious complications.

The following case illustrates all types of anoxia with fatality.

Case 1—A white, unmarried female, with bilateral pulmonary tuberculosis and secondary anemia, was treated by pneumothorax. The last pneumothorax was performed July 14, 1938, when 375 cc of air was introduced into the left pleural spaces. Adenoidectomy was performed July 15, 1938, with nembutal $1\frac{1}{2}$ gr morphine sulphate $\frac{1}{6}$ gr, and atropine $\frac{1}{200}$ gr as preoperative medication and nitrous oxide-oxygen anesthesia. The anesthesia lasted only 20 minutes but obvious cyanosis persisted throughout. The patient's condition was satisfactory when she was returned to her room an hour later but she was still unconscious and cyanotic. One hour later respirations became labored and soon stopped. *Anatomic Diagnosis* Asphyxia—blood uncoagulable, fibrocasseous tuberculosis, bilateral, chronic salpingitis. In this case the pneumothorax 24 hours previously and the nitrous oxide would account for anoxic anoxia, the secondary anemia for anemic anoxia, the surgical procedure for the low blood pressure and stagnant anoxia, and the preoperative medication nembutal and morphine for histotoxic anoxia.

The stagnant type of anoxia is well illustrated by two cases of splanchnic resection for hypertension. The procedure resulted in immediate reduction of systolic blood pressure, in the first case of 158 points and in the second of 116 points.

Case 2—White, female, age 45, married, no children. Complaint Dizziness. Present illness Approximately one year ago began having intermittent attacks of dizziness and vomiting. Last attack three weeks ago. Past history Pelvic operation in 1926. *Physical Examination* Heart enlarged, heart sounds roughened. Vessel walls moderately thickened. Blood pressure 214/142, pulse 104. Red blood count 4,340,000, hemoglobin 11.1 Gm. Urine Specific gravity 1.018, trace of albumin. Wassermann negative. Phthalein test 52 per cent in two hours. *Impression* Essential hypertension, cardiac hypertrophy, retinal hemorrhages, generalized arteriosclerosis. Transferred to Neurosurgery for splanchnic resection, bilateral.

Preoperative preparation Morphine sulphate $\frac{1}{4}$ gr, scopolamine $\frac{1}{100}$ gr. Operation, July 15, 1937. Duration of operation three and one-half hours. Blood pressure at beginning of operation 225/110, at end of operation 100/90. Returned from operation in fairly good condition. Pulse regular, rate 82, respirations 24, blood pressure 67/53. Twenty-four hours after operation, pulse 92, respirations 24, blood pressure 128/72. Drowsy, had difficulty in swallowing and speaking. Left facial paralysis. *Impression* at this time Cerebral anemia as the result of marked and sudden reduction of blood pressure. July 20 Facial paralysis persists and weakness is present in left lower extremity. Also blurring of vision. July 22 Patient still mentally confused. July 25 Blood pressure 165/105. Paralysis somewhat improved. Discharged the fourteenth day.

Case 3—White, female, age 51. Complaint Headaches, dizziness and nausea. Present illness Has been told frequently that she has high blood pressure. Past history Frontal and temporal headaches, has had "nervous breakdown." *Physical Examination* Undernourished and pale. Heart moderately enlarged. Blood pressure 256/150. Arterial walls thickened. Red blood count 3,850,000, hemoglobin 12.2 Gm. Phthalein 28 per cent in two hours. *Impression* Hypertension, generalized arteriosclerosis, mitral heart disease, spastic colon. Transferred to Neurosurgery for operation.

Preoperative preparation 4.7 mg avertin. Operation, January 9, 1937, under nitrous oxide. Bilateral splanchnic resection. Blood pressure at beginning of operation 236/130,

at end of operation 150/100 Returned from the operation in fair condition Pulse 76, respirations 22, blood pressure 120/90 January 10 and 11 Condition fairly good Blood pressure 140/86 January 12 Rales at both lower lobes *Impression* Pulmonary edema January 14 Patient unconscious January 24 Chest condition improved, no cyanosis Muttering delirium February 23 Discharged from hospital July 24 Patient in wheel chair Definite mental confusion Talked very little, did not recognize doctors, did not know where she was and did not answer questions satisfactorily Agitated and restless Blood pressure 150/110

Several types of anoxia are possible in the last case, but in view of observations to be presented later it is felt that the histotoxic type produced with the preoperative sedation of 12 gr of sodium amytal was the predominant factor

Case 4—Colored, female, age 32 Complaints Pelvic pain Physical examination reveals salpingo-oophoritis, bilateral, cystic right ovary, multiple fibroids of uterus Admitted to Gynecologic Service for operation, August 31, 1932

Preoperative orders include sodium amytal 3 gr, 10 P M, sodium amytal 6 gr, 6 30 A M, sodium amytal 3 gr, 8 15 A M, when called to operating room Operation performed under ether, oxygen and ethylene Operation Appendicectomy, hysterectomy, and bilateral salpingo-oophorectomy, lasting one hour and 25 minutes Following the operation the patient received pantopon 1/3 gr q 3 h, glucose 10 per cent and normal saline intravenously Consciousness was not regained following the operation, and a neurologic consultation resulted in a diagnosis of protracted ether narcosis September 10 Threshold of consciousness seemed to be slightly raised but motor coordination in the right lower extremity was disturbed September 14 Right-sided hemiparesis was evident September 15 Transferred to Neurologic Service for treatment By October 1, there was some improvement, patient was conscious but answers to questions were unintelligible Discharged from hospital, January 13, 1933, four and one-half months after operation, with some improvement in speech but with residual paralysis on right side *Final Diagnosis* Hemiplegia right (residual from prolonged narcosis)

These cases not only illustrate the various types of anoxia resulting in serious complications but they demonstrate that such complications may readily occur without either cardiovascular or respiratory failure during the anesthetic It is fully recognized that cessation of respiration or circulation for five or ten minutes may produce extensive degenerative changes in the central nervous system and perhaps other organs However, the data presented here emphasize that similar changes may result from reduction of oxygen tension, transportation or utilization, without interruption of respiration or circulation

For convenience in considering the anesthetics most commonly used in our institution they may be divided into seven groups Ether, ethylene and oxygen, cyclopropane and oxygen, nitrous oxide and oxygen, avertin, procaine (spinal), evipal and other barbiturates Much of the current work, including our own, on anesthesia is pure animal experimentation, but the observations on patients to be reported were made during the routine operative procedure, hence it is impossible to give results on the anesthetic agents alone, uninfluenced by the factor of preoperative medication In view of this, the barbiturates which are now frequently used preoperatively as sedatives and narcotics will be discussed first

The pharmacologic action of the barbituric acid compounds is described by Edmonds and Gunn¹⁰ as being essentially sedative and hypnotic, and Keeser and Keeser¹¹ found that they tend to localize in the diencephalon rather than the cerebral hemispheres. In addition to the cerebral action, a fall in body temperature, respiratory depression and an initial circulatory depression are usually noted. As intravenous anesthetics they are considered dangerous because the necessary dosage approaches the lethal one. For pre-operative medication, only the short acting preparations are to be employed if pulmonary complications resulting from prolonged respiratory depression and postoperative manias are to be avoided.

TABLE I

EFFECT OF PREOPERATIVE MEDICATION ON RESPIRATION OF CEREBRAL CORTEX

No	Amount of Drug	Q O ₂ in Cm Per Mg Dry Weight Per Hour		Percentage Decrease
		During	After	
	<i>Seconal 5%</i>			
1	2 I cc	1 6224	2 2702	28
2	2 I cc	1 4624	2 0455	28
	<i>Nembutal 3 33%</i>			
3	1 2 cc	2 8607	3 7616	23
4	1 6 cc	3 2421	3 8735	16
	<i>Morphine</i>			
5	½ Gr	2 6474	3 4721	23
6	½ Gr	2 330	3 0452	23
	<i>Sod Amytal 10%</i>			
7	0 8 cc	2 6471	3 3658	21
8	1 0 cc	2 398	3 3416	28

TABLE II

EFFECT OF PENTOBARBITAL NARCOSIS UPON BRAIN METABOLISM

(Av Three Dogs)

Blood Gas Analysis	Normal Unanesthetized	Pentobarbital* Narcosis	
		0 5 Hr	4 Hrs
Carotid Artery			
O ₂ content	16 9	12 4	15 5
O ₂ capacity	18 2	18 4	18 4
O ₂ saturation	93 3	68 8	84 6
CO ₂ content	40 6	49 0	42 5
Jugular Vein			
O ₂ content	14 0	10 3	12 9
CO ₂ content	45 4	51 4	45 0
O ₂ utilized	2 9	2 1	2 6
(AO ₂ -VO ₂)			
CO ₂ produced	5 4	1 1	2 5
(VCO ₂ -ACO ₂)			

* 30 to 35 mg per Kg body weight intravenous

It is interesting to hear the pharmacologists warn against pulmonary and cerebral complications, since cerebral necrosis and hemorrhagic pneumonia have been described in our earlier communications^{12,13} in both the experimental animal and patients when given fever therapy under heavy barbiturate sedation. Similar lesions have been produced in animals with these preparations alone. Jowett and Quastel¹⁴ have shown that luminal and evipal decrease or abolish the utilization of oxygen by brain slices. This work has been recently confirmed and extended in our laboratories working with sublethal doses of popular barbituric acid derivatives (Table I). Comparable inhibition of oxidation in liver, kidney and muscle by narcotics has been demonstrated also by Jowett and Quastel¹⁴.

TABLE III

Evipal Narcosis
Dosage 60 to 70 Mg Per Kg

Dog	Arterial Blood Oxygen 0.5 Hr		
	Cont	Cap	Sat
1	12.8	20.1	63.8%
2	16.5	19.6	84.0
3	11.5	15.1	76.6
4	13.2	15.9	83.4
5	14.3	17.5	81.5
6	11.8	15.5	76.0
Average	13.3	17.2	79.2

TABLE IV

Seconal Narcosis
Dosage 10 to 15 Mg Per Kg

Dog	Arterial Blood Oxygen 0.5 Hr		
	Cont	Cap	Sat
1	15.4	18.3	82.0%
2	14.5	16.9	86.3
3	11.3	15.3	74.0
4	12.8	18.1	70.8
5	12.9	15.7	82.2
6	13.5	16.2	83.0
Average	13.4	16.7	79.7

Brain metabolism *in vivo* under pentobarbital narcosis is shown in Table II. The oxygen content at the end of 30 minutes in the carotid artery is decreased 25 per cent, the oxygen capacity remains the same, the oxygen saturation is reduced 24 per cent, and the CO₂ content is increased 20 per

cent In the jugular vein, 30 minutes after administration, the oxygen content is reduced nearly 33 per cent and the CO₂ content has increased 10 per cent The oxygen utilized fell 28 per cent and the CO₂ produced fell 80 per cent

TABLE V
Sodium Pentobarbital Narcosis
Dosage 30 to 35 Mg Per Kg I V

Dog	Arterial Blood Oxygen					
	0.5 Hr			4 Hrs		
	Cont	Cap	Sat	Cont	Cap	Sat
1	13.1	20.2	65.2%	16.1	20.2	79.9%
2	13.1	17.3	78.3	14.9	17.3	86.3
3	11.1	17.6	63.0	15.4	17.6	87.7
4	14.6	18.3	79.8	16.4	18.3	89.9
5	14.7	19.0	77.5	16.3	19.0	86.2
6	11.2	16.8	66.0	14.8	16.8	88.2
Average	12.9	18.2	71.6	15.6	18.2	86.3

TABLE VI
Sodium Amytal Narcosis
Dosage 30 to 35 Mg Per Kg I V

Dog	Arterial Blood Oxygen								
	0.5 Hr			4 Hrs			7 Hrs		
	Cont	Cap	Sat	Cont	Cap	Sat	Cont	Cap	Sat
1	18.9	20.8	91.0%	18.9	20.8	91.0%	—	—	—
2	15.5	18.9	82.3	14.6	18.9	77.2	17.8	18.9	94.6%
3	16.0	18.9	84.8	13.1	18.9	69.6	17.4	18.9	92.4
4	14.5	17.4	83.7	15.7	17.4	90.6	—	—	—
5	22.1	24.7	89.5	—	—	—	—	—	—
6	21.3	24.5	87.1	—	—	—	—	—	—
Average	18.0	20.8	86.4	15.5	19.0	82.1	17.6	18.9	93.5

TABLE VII
Dial Narcosis
Dosage 1/2 Cc Per Kg I P

Dog	Arterial Blood Oxygen								
	1 Hr			2.5 Hrs			7 Hrs		
	Cont	Cap	Sat	Cont	Cap	Sat	Cont	Cap	Sat
1	13.9	16.5	84.6%	16.0	18.2	88.0%	18.7	20.0	93.5%
2	15.3	17.2	89.5	15.0	17.2	87.4	19.2	21.1	91.4
3	14.4	16.7	86.0	15.8	17.2	92.0	17.2	19.6	88.7
4	16.3	17.6	92.5	15.8	17.7	89.2	17.2	18.6	92.0
5	15.8	18.1	87.5	—	—	—	—	—	—
6	13.0	15.0	86.6	—	—	—	—	—	—
Average	14.7	16.8	87.7	15.6	17.5	89.1	18.0	19.8	91.4

Tables III, IV, V, VI and VII, showing arterial blood values in the dog under therapeutic doses of evipal, seconal, sodium pentobarbital, sodium amytal and dial, demonstrate that there is a consistent depression of the oxygen saturation ranging from 10 to 30 per cent with the lowest values produced by the shorter acting evipal, seconal and sodium pentobarbital

TABLE VIII
SECONAL GR 6

Patient	Age	Duration Min	Arterial Blood Oxygen			Blood Pressure	
			Cont	Cap	Sat	Normal	Sedat
N F	55	75	17 8	22 3	79 7%	158/70	150/60
V B	16	30	16 6	17 7	93 5	120/80	116/80
L K	60	30	18 2	19 9	91 5	212/110	185/106
B W	32	30	14 0	16 0	87 8	120/70	110/80
I R	31	90	18 1	21 7	83 5	116/70	115/85
M W	51	90	15 4	17 8	86 5	140/90	112/80
M R	41	30	18 2	21 0	86 7	150/82	128/100
M B	19	30	16 7	19 3	86 5	124/82	120/80
B C	60	45	12 4	14 5	85 8	158/80	144/88
S K	64	60	17 5	20 0	87 9	140/80	114/70
M B	20	60	16 0	18 1	88 6	120/70	

TABLE IX
CYCLOPAL GR 10

Patient	Age	Duration Min	Arterial Blood Oxygen			Blood Pressure	
			Cont	Cap	Sat	Normal	Sedat
M H	54	60	17 1	19 7	86 5%	142/75	102/70
M B	54	90	16 4	18 3	89 5	175/90	120/70
J H	29	60	15 9	19 0	83 7	135/80	115/75
E B	47	120	7 8	10 5	74 7	136/76	130/78
C R	51	45	16 2	20 3	79 8	140/96	140/96
E H	32	30	12 9	15 9	81 2	—	—
A B	28	30	18 6	21 0	88 5	—	—

Tables VIII and IX illustrate the effect of seconal and cyclopal respectively, given as preoperative medication on the oxygen saturation of the arterial blood and blood pressure. There is a uniform reduction in the oxygen saturation of from 5 to 20 per cent and usually a reduction in blood pressure ranging from 0 to 40 points systolic and 0 to 20 points diastolic.

From these data it seems clear that the barbiturate derivatives in moderate dosage produce slight to severe anoxia. This anoxia is due to respiratory depression (anoxic anoxia), circulatory depression (stagnant anoxia) and reduction of cellular respiration (histotoxic anoxia). Within the therapeutic range, histotoxic anoxia is most important in barbiturate sedation or narcosis, since brain slices have the utilization of oxygen reduced 16 to 28 per cent and the brain *in vivo* has its oxygen utilization reduced 28 per cent and its CO₂ produced reduced 80 per cent.

Avertin or triobromethanol has the chemical structure of ethyl alcohol with the substitution of three bromine atoms, and its narcotic effect is comparable to that of chloroform, according to Sollmann¹⁵ The preparation usually employed is avertin solution, that is one Gm of avertin dissolved in one cc of amylene hydrate, which is also an active narcotic The pharmacologic action from clinical dosage includes marked depression of the respiratory center with decrease in rate and diminished response to CO₂ Paissions,¹⁶ Greer,¹⁷ and Kennedy¹⁸ show that the blood pressure may be sharply depressed about eight minutes after administration due to vasodilatation, decrease in blood volume and depression of the heart Table X shows the reducing effect of avertin solution on the oxygen utilization of brain slices ranging from 10 to 14 per cent

TABLE X
EFFECT OF PREOPERATIVE MEDICATION ON RESPIRATION OF CEREBRAL CORTEX

No	Amount of Drug <i>Empal</i> 10% <i>Avertin</i> 1 5%	Q O ₂ in Cm Per Mg Dry Weight Per Hour		Percentage Decrease
		During	After	
1	2 0 cc	1 9268	2 4151	22
2	1 5 cc	1 9288	2 3822	19
3	1 0 cc	2 4872	3 0971	19
4	1 2 cc	2 8081	3 5693	21
5	2 0 cc	2 0549	2 545	19
6	35 cc	3 1294	3 4673	9 7
7	40 cc	2 819	3 2924	14
8	42 cc	2 9745	3 3807	12

TABLE XI
Avertin Narcosis
Dosage 180 Mg Per Kg

Dog	Arterial Blood Oxygen		
	0 5 Hr		
	Cont	Cap	Sat
1	13 7	17 1	80 2%*
2	19 0	21 4	88 6
3	17 9	20 1	89 4
4	19 5	21 5	91 2
5	15 3	22 3	68 5†
6	17 1	20 4	84 1
Average	17 0	20 4	83 6

* N B P 170/90, narcosis 100/55

† R = 4 min, deep narcosis

Table XI shows the reduction in the oxygen saturation of the arterial blood in avertin narcosis in the dog resulting from 180 mg per Kg. The percentage of reduction varies from 3 to 25 per cent, the average being 10 per cent. The first animal exhibited a fall of 70 points in systolic blood pressure and 35 points in diastolic blood pressure. In the fifth animal, the respiratory rate fell to four per minute and was accompanied by deep narcosis and the sharpest reduction in the oxygen saturation of the arterial blood.

TABLE XII
AVERTIN NARCOSIS

Patient	Age	Sedation Avertin	Duration Min	Arterial Blood Oxygen			Blood Pressure	
				Cont	Cap	Sat	Normal	Anesth
J B	32	90 mg /Kg	30	17.0	19.2	88.7%		
M L	35	80 mg /Kg	45	18.0	20.4	88.0	202/134	140/90
M C	45	70 mg /Kg	60	18.9	20.7	91.2	160/60	180/100
T H	61	70 mg /Kg	30	16.9	18.9	89.2	150/85	100/60
B H	54	80 mg /Kg	30	15.4	17.6	87.7	126/70	90/60
H P	30	80 mg /Kg	45	16.6	19.5	85.2	124/70	120/50
L Mc	42	70 mg /Kg	45	13.3	17.6	75.5	110/60	100/60
L B	66	70 mg /Kg	30	13.5	14.8	91.6	140/60	100/60
T de P	28	80 mg /Kg	30	15.0	16.7	89.6	130/82	100/80
A C	32	85 mg /Kg	20	17.5	19.8	88.4	156/86	150/80

Table XII shows the oxygen saturation of ten patients under avertin anesthesia, ranging from 3 to 20 per cent below normal. The blood pressures were taken after the critical period, eight minutes following administration, but show consistent reduction in systolic pressures ranging from 4 to 62 points, and in diastolic pressures ranging from 0 to 44 points. It is to be noted that none of these patients received other preoperative medication which might account for the relatively good record shown. The anoxia in this instance is charged to depression of the respiratory center with slowing of the rate (anoxic anoxia), to the reduction in blood pressure and vasodilatation (stagnant anoxia) and, to a small degree, to histotoxic anoxia, as the utilization of oxygen by brain slices is depressed from 10 per cent to 14 per cent, or less than half seen with the barbiturates.

The recent contributions on spinal anesthesia by Seevers and Waters,⁶ Schubert,¹⁹ Shaw, Steele and Lamb,²⁰ and Nowak and Downing²¹ make it impossible to add anything except observations upon patients under actual operative conditions.

All of our patients (Table XIII) had preliminary sedation with morphine sulphate or barbiturates. Some of the oxygen saturation values are within the normal range and the greatest reduction was 10 per cent. In view of the data presented above, the slight changes are attributed to the effect of preoperative medication alone. There is a fall in blood pressure in each case which is routinely combated by ephedrine and oxygen inhalations. Seevers

and Waters⁶ observed that "a considerable decrease in alveolar, as well as in arterial and venous blood oxygen occurs, with a corresponding increase in CO₂" This result they attribute to "initial decrease in peripheral resistance to blood flow, vasomotor nerve and skeletal muscle paralysis, decrease in minute volume respiration accompanying intercostal nerve paralysis, inadequate oxygenation of blood, diminished minute volume blood flow, progressive loss of vascular tone over the whole body and acute cardiac incompetence, and failure of the medullary respiratory mechanism" Schubert¹⁹ found no definite changes in oxygen consumption in man, the arteriovenous difference was increased, and the cardiac output and blood pressure fell Shaw, Steele and Lamb,²⁰ in dogs, found a perfectly saturated arterial blood and a lowered oxygen content of the venous blood or an increased arteriovenous difference indicating stagnant anoxia They believe that this anoxia will vary with the extent of the area anesthetized or the magnitude of the vasoconstrictor paralysis and vasomotor compensation Nowak and Downing,²¹ working with cats under light ether anesthesia, found spinal anesthesia did not depress the arterial oxygen, however, the venous oxygen content was reduced, resulting in an increased arteriovenous oxygen difference They suggest that fatal accidents are due to paralysis of the phrenic mechanism or respiratory center, or both There is substantial agreement between three of the four workers quoted, and their conclusion that there is no substantial reduction in arterial blood oxygen when the cardiovascular depression is combated, corresponds with our observations in anesthetized patients

TABLE XIII
SPINOCAINE (SPINAL)

2.5 TO 3 Cc

Patient	Age	Sedation	Dura- tion Min	Arterial Blood Oxygen			Blood Pressure	
				Cont	Cap	Sat	Normal	Anesth
L K	31	Nembutal Gr 1½ M S Gr ¼	60	21 2	22 4	94 5%	134/78	120/80
S S	56	M S Gr ¼	90	16 4	19 3	83 2	130/80	88/50
F T	53	Seconal Gr 3	60	18 9	20 4	92 7	126/82	100/70
H L	22	M S Gr ¼	60	21 3	23 7	89 9	140/86	130/90
G P	34	M S Gr 1/6	90	20 6	22 6	91 5	125/75	90/70
S M	32	Seconal Gr 3	120	18 4	21 1	87 5	120/90	86/60
G S	39	Seconal Gr 3	90	20 3	22 7	89 4	106/70	100/70
J B	41	Seconal Gr 3	120	19 0	21 8	86 7	140/92	100/70 Eph 150/90
A S	43	Seconal Gr 3	15	16 1	19 0	84 9	140/76	80/50 Eph 110/80
O C	32	Seconal Gr 3	60	19 6	21 2	88 0	118/20	100/66

Nitrous oxide was the first inhalation anesthetic and it acts partly by direct narcotic effect upon the central nervous system, but to a greater extent through the exclusion of oxygen The action is perhaps best illustrated by Clark (from Sollmann¹⁵) in Table XIV

When nitrous oxide is combined with air or oxygen it produces almost a pure anoxic anoxia by the exclusion of oxygen from the inspired mixture When combined with preoperative medication the latter brings in both the

TABLE XIV

Vol %		Degree of		
N ₂ O	O ₂	Depth of Anesthesia	Asphyxia	Relaxation
80	20	Subconscious analgesia	None	None
86	14	Complete analgesia	None	None
89	11	Partial anesthesia	Slight	Slight
94	6	Complete anesthesia	Dangerous	Partial

TABLE XV
NITROUS OXIDE AND OXYGEN

Patient	Age	Sedation	Duration Min	Arterial Blood Oxygen			
				Mother			Baby
				Cont	Cap	Sat	Sat
K T	22	None	140	12 1	19 4	62 4%	49 9%
B A	40	Seconal Gr 6	15	16 2	19 4	83 2	
M W	52	Cyclopal Gr 10	20	17 2	20 1	85 7	
R T	18	Pentobarb Gr 13½ (24 hrs)	40	12 1	18 6	65 2	
M S	34	Pentobarb Gr 7½ Scopol Gr 1/100	60	12 1	15 7	77 2	
S B	44	Pentobarb Gr 6	30	15 9	21 0	76 1	
D F	25	Pentobarb Gr 6 Scopol Gr 1/100	30	6 2	11 6	53 3	
M V	25	Pentobarb Gr 4½ Scopol Gr 1/100	45	9 9	19 6	50 5	
C S	49	Seconal Gr 6	60	17 3	18 5	93 6	
E B	22	Pentobarb Gr 6 (3 hrs)	20	12 6	16 5	76 4	
N M	29	Pentobarb Gr 6 Scopol Gr 1/150	15	13 8	18 9	72 9	48 9
L H	22	Pentobarb Gr 4½ Scopol Gr 1/200	20	11 8	14 5	81 0	
F M	24	Pentobarb Gr 6 Scopol Gr 1/150 M S Gr 1/6	30	14 8	17 2	85 9	
A T	28	Pentobarb Gr 1½	20	14 7	18 8	78 2	50 0
J S	21	Seconal Gr 4½	30	12 5	15 2	82 6	61 2
U R	43	Pentobarb Gr 7½ (24 hrs) Pentobarb Gr 6 (11 hrs) Scopol Gr 1/200, 1/200, 1/200	30	12 4	18 0	68 7	
M D	24	No sedation	50	15 6	18 7	83 0	76 0
H V P	38	Seconal Gr 6 (4-6 hrs) Scopol Gr 1/150, 1/150 (3-8 hrs)	40	11 5	15 5	74 6	52 0
M M	28	Pentobarb Gr 4½ (1 hr)	20	16 5	18 3	90 0	64 5
V D	20	Pentobarb Gr 4½ (7 hrs) Scopol Gr 1/150, 1/150 (5 hrs)	40	13 7	16 6	82 7	62 3

stagnant and histotoxic factors Table XV represents arterial bloods on obstetric patients under nitrous oxide anesthesia at the time of delivery (second stage) and the cord blood of the newborn infants All the mothers had preoperative medication, usually one of the barbiturates with or without scopolamine The oxygen saturation of the arterial blood was reduced from 0 to 45 per cent, with the greatest reduction found with relatively large doses of pentobarbital and scopolamine The average reduction in the oxygen saturation of 14.4 is moderate as compared with other groups, but the most significant and dangerous aspect is the irregularity and extreme reduction in seven out of the 20 cases Raginsky and Bourne,⁷ in a series of 14 patients receiving nitrous oxide for extractions and other short operations, found an average reduction in the oxygen saturation of the arterial blood of 25 per cent, but three cases had oxygen saturation of below 55 per cent The saturation of the cord blood in most instances is well correlated with the mother's arterial blood

Ethylene was introduced as a clinical anesthetic, in 1923, by Luckhardt and Cartei,²² and Luckhardt and Lewis.²³ Sollmann¹⁵ states that it is an aliphatic narcotic of low activity but with rapid action and recovery Full anesthesia may be induced with 90 per cent ethylene and 10 per cent oxygen After induction satisfactory relaxation may be maintained with 80 per cent ethylene and 20 per cent oxygen It is, therefore, unnecessary to produce anoxia to obtain anesthesia and the color remains good In the arterial blood of our cases (Table XVI) the oxygen saturation in only one instance was reduced below the level expected in view of the preoperative medication with barbiturates and morphine sulphate

TABLE XVI
ETHYLENE AND OXYGEN

Patient	Age	Sedation	Duration Min	Arterial Blood Oxygen		
				Cont	Cap	Sat
S K	20	Cyclopal Gr 10	30	9 2	15 2	60 4%
J G	42	Cyclopal Gr 10	30	13 6	16 0	84 9
A L	15	M S Gr 1/6	60	19 1	21 3	89 7
A H	22	M S Gr 1/6	60	17 2	19 1	90 2
M K	40	Seconal Gr 6	30	15 4	17 1	90 1
A K	39	M S Gr 1/4	30	13 9	17 8	78 3
C P	62	Cyclopal Gr 10	30	17 6	19 7	89 0
M G	32	Seconal Gr 6	30	16 4	20 2	81 3
R E	40	Nembutal Gr 6	10	15 7	17 8	87 9
B R	59	Nembutal Gr 6	15	20 0	22 2	90 2

Cyclopropane was proposed as an anesthetic by Lucas and Henderson,²⁴ in 1929 Since that time, a number of clinical reports indicate its increasing use for induction and more lately from general anesthesia Sollmann¹⁵ states that 7.4 per cent produces mild anesthesia, 13 per cent is suitable for abdominal operations and 23 per cent is sufficient for deep anesthesia Any surgical

procedures may, therefore, be undertaken with the patient getting 77 per cent oxygen

TABLE XVII
CYCLOPROPANE

Patient	Age	Sedation	Duration Min	Arterial Blood Oxygen			Blood Pressure	
				Cont	Cap	Sat	Normal	Anesth
G K	47	M S, Gr 1/6	40	15 8	17 7	89 3%	150/90	110/60
S V	21	Seconal Gr 4½	15	14 4	16 3	88 2	—	—
M B	44	Seconal Gr 3	15	21 2	22 1	95 0	120/80	110/76
J W	43	M S Gr 1/6	90	18 5	19 7	92 8	120/80	120/80
M R	33	Seconal Gr 6	30	10 8	11 5	94 0	150/80	120/80
K L	25	Seconal Gr 4½	30	16 8	18 8	89 6	118/68	110/70

In Table XVII, the arterial blood oxygen saturation taken during anesthesia shows only slight depression despite the fact that all had preoperative medication with morphine sulphate or seconal. One report of postanesthetic encephalopathy following cyclopropane has been made by Gebauer and Coleman,²⁵ who conclude that tissue or cellular anoxia is the probable cause of the encephalopathy and death. Their conclusion seems logical, but preoperative medication of sodium amytal 3 gr and morphine sulphate ¼ gr, the type (thoracoplasty) and length of the operation, and the circulatory depression evidenced by low blood pressure and the rapid pulse should be considered the principal precipitating factors rather than the cyclopropane.

DISCUSSION—With this study and comparison of the various commonly used narcotics and anesthetics, it becomes apparent that anoxia of some degree and of one or more types usually occurs as a result of their administration. Ordinarily this anoxia is not of sufficient degree to endanger the patient's life or tissues. However, the cases cited here, those of Couville,¹ Lowenberg, Waggoner and Zbinden,²⁶ Gebauer and Coleman,²⁵ O'Brien and Steegmann,²⁷ and Steegmann,²⁸ doubtless represent only a small percentage of those that will shortly be recorded now that the clinical picture, the pathogenesis and the pathology are identified and are rapidly becoming clarified.

Evipal and the other barbiturates in therapeutic doses produce relatively severe anoxia by respiratory depression (anoxic type), circulatory depression (stagnant type) and reduction of cellular respiration, especially in the brain (histotoxic type). Only the elimination of the barbiturates in large preoperative doses and as anesthetics will prevent anoxia.

Avertin, or tribromethanol, like the barbiturates, depresses both respiration and circulation, resulting in anoxic and stagnant anoxia, but there is relatively little histotoxic anoxia. If measures were taken to combat the early fall in blood pressure and the decreased respiratory rate, the anoxia could be reduced to a minimum.

Spinal anesthesia produces marked circulatory depression through paralysis of the vasoconstrictors in the anesthetized area, leading to stagnant anoxia.

If this vasodilatation and fall in blood pressure is effectively overcome, there is little or no anoxia seen from the spinal anesthesia alone. However, this holds only if the preoperative medication is avoided or kept at minimum levels.

Nitrous oxide-oxygen anesthesia of complete grade requires the reduction of the oxygen in the inspired mixture below maintenance levels (about 6 per cent), therefore, pure nitrous oxide anesthesia predicates anoxic anoxia. It is used only in short anesthesia such as extractions. In longer procedures preoperative medication with barbiturates or morphine sulphate is the rule. Thus both stagnant and histotoxic anoxia are added to make a potentially dangerous total. Apparently little can be done to reduce this risk as preoperative medication is necessary. The nitrous oxide cannot be reduced below the borderline of anoxia, and even with the most cautious administration some of the cases show the arterial blood oxygen saturation at unexpectedly and dangerously low percentages of 50 to 55.

Ethylene and cyclopropane, especially the latter, offer good margins of safety as far as the percentage of oxygen in the inspired mixture is concerned. Anoxia need occur only through heavy preoperative medication or the use of unnecessarily high percentages of the anesthetic gas.

Courville,¹ Lowenberg, Waggoner and Zbinden,²⁸ and Steegmann²⁸ have already described the brain pathology occurring after nitrous oxide, avertin and cyclopropane anesthesia. The changes noted by these observers are essentially the same and they correspond closely with those recorded by Gildea and Cobb²⁹ after experimental ligation of the cerebral vessels, and by one of us¹³ following fever therapy with heavy sedation, after large doses of barbiturates, and in acute alcoholism.

The pathologic changes may be roughly grouped into the acute and subacute to chronic. The acute changes may be confined to those in experimental animals or man surviving from a few hours to 24 hours after the production of anoxia. Here marked engorgement of the pial and cerebral vessels is found grossly. The lungs are usually voluminous and of increased density. On section the lung parenchyma is edematous and congested. The other organs show congestion only. Microscopically, the acute changes in the brain are characterized by pericellular and perivascular edema, shrinkage of the pyramidal cells of the cortex and the ganglion cells, and cuff hemorrhages, especially in the basal nuclei. The histologic changes in the lung are typified by the diffuse hemorrhagic infiltration (hemorrhagic pneumonia). At times small hemorrhages may be found in the cortex of the adrenal and in the cortex of the kidney.

In the subacute to chronic cases, that is, in those surviving 24 to 48 hours or longer, all the pathologic changes of the acute phase may be noted in the gross, plus areas of necrosis and hemorrhage. These areas have been called devastation necrosis by Gildea and Cobb²⁹ and are found most frequently in the basal nuclei. There may be zonal necroses in the cortex, as noted by Courville,¹ or of entire lobes, as noted in the cerebellum of one of our cases.

The changes in individual cells are more advanced, being seen in stages of liquefaction, lipoidal degeneration and calcification

The lung at this stage either shows resolution of the hemorrhagic lesion of the acute period, or it has gone on to frank consolidation of lobular or lobal distribution. The liver may show central or midzonal necrosis with hemorrhage. The kidney may still show hemorrhage and in addition tubular degeneration

CONCLUSIONS

(1) Anoxia may usually be demonstrated during anesthesia induced by present-day methods

(2) Narcotics, particularly morphine and barbiturate derivatives in moderate to large doses, tend to produce anoxia, especially of the histotoxic type

(3) Destruction of individual cells, vital organs and life itself is most apt to result when a severe histotoxic anoxia is accentuated by one or more of the other types, anoxic, stagnant or anemic anoxia

(4) Full consideration of anoxia as a source of surgical complications should reduce preoperative narcotics to a minimum, promote the use of anesthetics which allow adequate oxygen in the inspired air, and emphasize the necessity of maintaining the blood pressure and respiration at near normal levels

REFERENCES

- ¹ Courville, C B. Asphyxia as Consequence of Nitrous Oxide Anesthesia. *Medicine*, **15**, 129, 1936
- ² Henderson, Y. Fundamentals of Asphyxia. *J A M A*, **101**, 261, 1933
- ³ Barcroft, W D. Anoxemia. *Lancet*, **2**, 485, 1920
- ⁴ Schmidt, C F. Recent Studies on Some Physiological Phenomena Related to Anesthesia. *Current Res Anesth and Analg*, **17**, 24, 1938
- ⁵ Shaw, J L, Steele, B F, and Lamb, C A. Effect of Anesthesia on the Blood Oxygen. I. A Study of the Effect of Ether Anesthesia on the Oxygen in the Arterial and in the Venous Blood. *Arch Surg*, **35**, 1, 1937
- ⁶ SeEVERS, M H, and Waters, R M. Respiratory and Circulatory Changes During Spinal Anesthesia. *J A M A*, **99**, 961, 1932
- ⁷ Raginsky, B B, and Bourne, W. Cyanosis in Nitrous Oxide-Oxygen Anesthesia in Man. *Canad M A J*, **30**, 518, 1934
- ⁸ Courville, C B. The Pathogenesis of Necrosis of the Cerebral Gray Matter Following Nitrous Oxide Anesthesia. *ANNALS OF SURGERY*, **107**, 371, 1938
- ⁹ Brown, Easson, Lucas and Henderson. The Anesthetic Value of Nitrous Oxide Under Pressure. *J Pharmacol and Exper Therap*, **31**, 269, 1927
- ¹⁰ Edmonds, C W, and Gunn, J A. Cushman's Textbook of Pharmacology and Therapeutics. Tenth ed, Lea and Febiger, Philadelphia, 1934
- ¹¹ Keeser, E, and Keeser, J. Proof of Caffeine, Morphine and Barbituric Acid Derivatives in the Brain. *Arch exp Pathol u Pharmacol*, **127**, 230, 1928
- ¹² Hartman, F W. Lesions of the Brain Following Fever Therapy. *J A M A*, **109**, 2116, 1937
- ¹³ Hartman, F W, and Major, R C. Pathological Changes Resulting from Accurately Controlled Artificial Fever. *Am J Clin Pathol*, **5**, 392, 1935

- ¹⁴ Jowett, M, and Quastel, J H The Effects of Narcotics on Tissue Oxidations Biochem Jour, **31**, 565, 1937
- ¹⁵ Sollmann, T Manual of Pharmacology Fifth ed, W B Saunders, Philadelphia, 1936
- ¹⁶ Parsons, F B Avertin Brit Med Jour, **2**, 709, 1929
- ¹⁷ Greer, C C Avertin West Virginia Med Jour, **26**, 538, 1930
- ¹⁸ Kennedy, W P Avertin on Blood Pressure Edinburgh Med Jour, **37**, 142, 1930
- ¹⁹ Schubert, O O On the Disturbance of the Circulation in Spinal Anesthesia Acta Chir Scandinav, **78**, Suppl 43, 1, 1936
- ²⁰ Shaw, J L, Steele, B F, and Lamb, C A Effect of Anesthesia on the Blood Oxygen II A Study of the Effect of Spinal Anesthesia on the Oxygen in the Arterial and in the Venous Blood Arch Surg, **35**, 503, 1937
- ²¹ Nowak, S J, and Downing, V Oxygen and Carbon Dioxide Changes in Arterial and Venous Blood in Experimental Spinal Anesthesia J Pharmacol and Exper Therap, **64**, 271, 1938
- ²² Luckhardt, A B, and Carter Ethylene J A M A, **80**, 765, 1923
- ²³ Luckhardt, A B, and Lewis Ethylene J A M A, **81**, 1851, 1923
- ²⁴ Lucas, G H W, and Henderson, Y Cyclopropane Anesthesia Canad M A J, **21**, 173, 1929
- ²⁵ Gebauer, P W, and Coleman, F P Postanesthetic Encephalopathy Following Cyclopropane ANNALS OF SURGERY, **107**, 481, 1938
- ²⁶ Lowenberg, K, Waggoner, R, and Zbinden, T Destruction of the Cerebral Cortex Following Nitrous Oxide-Oxygen Anesthesia ANNALS OF SURGERY, **104**, 801, 1936
- ²⁷ O'Brien, J D, and Steegmann, A T Severe Degeneration of the Brain Following Nitrous Oxide-Oxygen Anesthesia ANNALS OF SURGERY, **107**, 486, 1938
- ²⁸ Steegmann, Albert T Encephalopathy Following Anesthesia Arch Neurol and Psychiat, **41**, 955, 1939
- ²⁹ Gildea, E F, and Cobb, S The Effects of Anemia on the Cerebral Cortex of the Cat Arch Neurol and Psychiat, **23**, 876, 1930

THE PRESENT STATUS OF SPINAL ANESTHESIA*

HAROLD L FOSS, M D , AND LEONARD F BUSH, M D

DANVILLE, PA

FROM THE DEPARTMENT OF SURGERY, THE GEORGE F GLISINGER MEMORIAL HOSPITAL, DANVILLE, PA

To STRICTLY follow the title of this paper would comprehend a survey of the use of spinal anesthesia throughout the civilized world and a summary of the opinions of all surgeons, of the present state of this means of rendering insensibility to pain—obviously an impossibility. One can, however, providing his experience with a method has been sufficiently extensive, arrive at certain conclusions, and, with a survey of a comprehensive literature, state what seems to be the modern evaluation of it. We have, therefore, attempted to sum up present day beliefs regarding an anesthetic technic over which there has probably been more controversy than has occurred in reference to all other anesthetics combined.

In a symposium such as this, in which nearly all modern forms of anesthesia are being considered, spinal as a procedure is of too great importance not to be also represented. Yet, bearing in mind that probably more has been said and written during the past ten years about it than about other methods, one is put to it to approach the subject from an original angle and to escape rehashing what has already been mentioned not once but a thousand times.

Nothing of much value can be added to what has been written with reference to the best drugs to employ and the best technics to be followed in their administration, to the question of indications or contraindications or to that of the selection of the types of patient and operation best suited to the procedure. All these subjects have been extensively dealt with. Much has, however, been contributed lately regarding certain dangers of spinal anesthesia.

Complications of Spinal Anesthesia—Veal and Van Weiden analyzed 30 immediate fatalities in some 33,000 cases in which the method was used in the Charity Hospital of New Orleans. All deaths occurred in the operating room or soon after the injection was made, so there was, in the minds of the authors, no question as to the responsibility of the anesthetic. In the latter half of the series, immediate deaths occurred once in every 1,244 cases. All but four of the deaths occurred with novocain, the authors stating that the risk rapidly rises with the increase of the dosage—yet in 21 of the deaths the dosage was 150 mg. or less.

Davis and Hale Haven carried out injections in dogs. Most marked pathologic change found was meningeal reaction present in a variable degree—an inflammatory reaction in the arachnoid with a thickening of the membrane.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

and collections of proliferated arachnoidal cells. Occasionally they found collections of polymorphonuclear cells but in no instance were bacteria discovered. Exudates were largely of the lymphocytic type. In animals killed 30 to 90 days after injection, organization with fibrotic scarring could be seen. The authors conclude that spinal anesthetic solutions are hemolytic as well as myelolytic and that, following injection, there is a varying degree of inflammatory reaction in the leptomeninges. Swelling and pigmentation of the axis-cylinders, occasionally with degenerative changes in the fiber tracts of the cord, occurs. Changes in the ganglion cells of the gray matter similar to those seen in retrograde or wallerian degeneration may frequently be demonstrated but these latter changes are, probably, not of a permanent nature.

Sise, in 1929, collecting the reports of deaths from spinal anesthesia in greater Boston for one year, states that a "rough estimate of the number of spinal anesthetics given during this period forces the conclusion that the death rate has not been better than one to one hundred." Compared with Sise's findings, however, we have the reports of Rygh and Bessesin, analyzing statistics of 250,895 spinal anesthetics with a mortality rate of 1 to 3,345. Obviously such wide discrepancies suggest a lack of standardization in the methods of statistical compilations—a factor which, all too frequently, enters the picture in our scientific investigations, often invalidating the conclusions.

Falk records that in a consecutive series of 260 anesthetics he had no mishap, however, with a change of services three fatalities occurred on the operating table in the next 154 cases—all apparently from acute respiratory failure. A routine dosage of 200 mg. was used in all cases, obviously one far too great.

Many writers have referred to the patient's individual susceptibility and cite, for example, sudden death from novocain injected into a tonsil. Certain transitory minor effects may well be attributed to a peculiar idiosyncrasy possessed by the patient, or, as has been assumed, to tissue sensitivity to cocaine derivatives.

There is, as pointed out by Harrison, a widespread impression that continued leakage from the puncture occurs and that leakage, by reducing pressure within the subarachnoid space, causes the headache. Introduction of air alone may cause intense headache. Harrison advocates the routine intravenous injection of glucose in the prevention of postoperative spinal headache, the "slight hydremia which the dextrose solution induces being sufficient to check the excessive absorption from the spinal canal—until recovery or until compensation can take place, thereby reducing the disturbance in cerebrospinal hydrostatics to so low a level that the headache does not appear."

Koster *et al* list the explanations of headache under (a) Seepage of cerebrospinal fluid, (b) irritative meningitis from the solution from skin contaminations, (c) alterations in the p_H of the solutions. Yet Koster and his associates conclude that any possible contamination from substances used in preparation of the skin plays no part in the production of headache, neither

does the factor of hypo- or hypertonicity. Koster found that the deliberate injection, with the anesthetic agent, of iodine or of trinitrophenol did not increase the incidence of postoperative headaches, neither did the use of tap water or distilled water in the place of saline solution.

Lindemulder concludes that procaine or its allied drugs have a definite toxic effect on the cord and spinal nerve roots which can be shown both clinically and pathologically.

Years ago, Spielmeyer, following injection of stovaine into the subarachnoid spaces of dogs and apes, found degeneration of the roots and the peripheral portions of the cord, and retrograde degeneration in the anterior horn cells. Lindemulder has described degenerative changes in the spinal anesthetics, while Van Lier and Wossidlo demonstrated the toxic effects of anesthetic substances on neural tissues. Lindemulder, Hyslop and Smith have recorded definite instances of neural damage following the administration of spinal anesthetics. Involvement of the cranial nerves is mentioned—abducens palsy seems to be the one most frequently mentioned. Trigeminal, facial and auditory nerve involvements have been referred to.

Kilman and Abbott have found stovaine to cause degeneration of the nerve roots at the periphery of the cord and retrograde changes in the anterior horn cells in dogs and apes. All anesthetics which contained procaine were shown to be myelitic and hemolytic. This was proven by the experimental work on dogs and postmortem examinations on patients who died following the use of spinal anesthesia.

They feel that other factors than the drug may be responsible, inserting the needle too far, after entering the dura, admixture of blood—with resulting fibrosis or leptomeningitis, the needle, striking the anterior wall, injuring veins, and causing bleeding into the cord.

Thompson reports eight fatalities occurring with the use of spinal anesthesia. Seven of these were, possibly, precipitated by the spinal. One patient died suddenly following the administration of the spinal, from no apparent cause other than the anesthetic.

Loeser reports five cases of peripheral neuritis following spinal anesthesia. All patients were discharged well but developed neuritis after long periods.

Anderson reports a case of trophoneurotic gangrene of an extremity following the use of spinal anesthesia, and reviews the literature listing six foreign authors who have described similar cases.

Hyslop, in discussing the nervous system sequelae of spinal anesthesia, stresses the fact that many symptoms may be due to trauma from the needle used. He questions aseptic meningitis or encephalitis as true entities and concludes that there is no evidence to show that cocaine or its derivatives produce permanent central nervous system damage. He does, however, mention the hemolytic and myelolytic actions of the drug.

Koster and Wientrob review 6,000 cases in which spinal was used, with nine deaths which might be attributed to the anesthesia. In none of these

cases did postmortem examination reveal any definite evidence that spinal anesthesia played any part

Personal Experiences—The great utility of spinal anesthesia under certain circumstances is recognized by nearly every surgeon. There are still a goodly number of agnostics, but their number is decreasing, about paralleling another phenomenon and one even more fortunate—a decrease in the number who have, heretofore, been unalterable advocates of the method as a routine

TABLE I
MORTALITY FOLLOWING 10,000 CONSECUTIVE OPERATIONS
(All Performed on Structures Below the Diaphragm)

5,000 Consecutive Operations Under Spinal Anesthesia

Deaths	351
Mortality	7.02%
Deaths in operating room	3
Percentage of deaths occurring in operating room to total hospital deaths under spinal	0.88%

5,000 Consecutive Operations Under General Anesthesia

Deaths	255
Mortality	5.1%
Deaths in operating room*	12
Percentage of deaths occurring in operating room to total hospital deaths under general anesthesia	4.7%

* Operating room deaths under general anesthesia show too high a figure—most occurred several years ago, when the anesthetic was straight ether

(Only two operating room deaths occurred in the last 3,000 operations, all performed under cyclopropane-ether)

TABLE II

DEATHS IN OPERATING ROOM IN 5,000 CONSECUTIVE OPERATIONS BELOW DIAPHRAGM (SPINAL)

Three Patients Who Died in Operating Room Under Spinal Anesthesia

Sex	Age	Pathology
1 F	52	Supravaginal hysterectomy Autopsy (1) Miliary tuberculosis, (2) chronic myocarditis, (3) fatty degeneration of the liver, (4) chronic nephritis, (5) atheroma of the aorta, (6) active pulmonary tuberculosis, (7) active tuberculosis of the spleen
2 M	59	Exploratory celiotomy Carcinoma of stomach with perforating ulcer, peritonitis (lived 15 minutes) No autopsy
3 M	35	Exploratory celiotomy Gastric ulcer (lived 30 minutes) Autopsy (1) Chronic myocarditis, (2) aortic stenosis, (3) hypertrophy and dilatation of heart

The authors believe that their experience and results have followed fairly closely those of men working in other clinics where spinal anesthesia is extensively used, and so set forth an account of their own conclusions as fairly representative, at least in this country, of the present status of spinal

SPINAL ANESTHESIA

TABLE III

OPERATIVE PROCEDURES IN WHICH DEATH OCCURRED

(Operations All Below Diaphragm)

	Spinal 5,000 Cases	General 5,000 Cases
Amputations	23	8
Appendicectomies	45	34
Exploratory celiotomies (Chiefly for carcinoma)	53	49
Herniorrhaphies (Strangulated)	28	9
(4 Nonstrangulated)		
Operations upon gallbladder and ducts	52	28
Operations upon kidney, bladder and prostate	32	35
Operations in pelvis	33	24
Operations upon stomach, intestines, <i>etc</i>	81	50
Miscellaneous	4	18
	<hr/>	<hr/>
Totals	351	255

TABLE IV

RATIO OF DEATHS FOLLOWING INHALATION ANESTHESIA (5,000)
TO THOSE FOLLOWING SPINAL ANESTHESIA (5,000)

	Spinal	General Anesthesia
In operating room	3	13
1st 12 hrs postoperative	15	26
2nd 12 hrs postoperative	22	24
3rd 12 hrs postoperative	34	13
4th 12 hrs postoperative	26	14
	<hr/>	<hr/>
Totals	100	90
After 48 hrs	251	165
	<hr/>	<hr/>
Total deaths	351	255
Mortality*	7.02%	5.1%
Hospital operative mortality as a whole		2.96%

(All were consecutive cases and all operations were performed on structures below the diaphragm)

* The 2 per cent mortality difference between spinal and ether in the above report is not significant. In a previous study of 2,000 consecutive spinal and 2,000 consecutive general cases, the mortality stood respectively 6.5 per cent and 6.8 per cent. In the last series, the more seriously ill and worst risk cases were handled under spinal, probably accounting for the slightly increased mortality.

Several years ago, the senior author⁵ compared the results following the administration of spinal to 2,000 consecutive patients with those following the administration of various forms of inhalation anesthesia to a like number, 4,000 operations in all, performed by himself in the same operating room.

and with the same operating room personnel, on structures below the diaphragm. The hospital mortality was found to be equal for the two methods. In the present paper, a series of 5,000 consecutive operations under spinal is taken as a text. All operations were performed by the senior author or by his assistant, in the same operating room, and under like conditions. The patients were followed, during their convalescence, with that degree of care permitted only the surgeon who lives constantly in the institution with his patients, and, therefore, in the closest touch with their progress.

TABLE V

ANALYSIS OF DEATHS IN OPERATING ROOM*

(5,000 Consecutive General Anesthetics)

Twelve Patients Who Died in Operating Room Under General Anesthesia

	Sex	Age	Operative Procedure
1	F	35	Suturing traumatic rupture of the uterus, advanced peritonitis
2	F	29	Salpingo-oophorectomy, cardiorespiratory failure
3	F	66	Appendicectomy, gangrenous appendicitis, cardiorespiratory failure, peritonitis
4	M	60	Exploratory celiotomy (chronic cholecystitis and pancreatitis), chronic myocarditis, cardiac failure
5	M	62	Closure—perforated duodenal ulcer, generalized peritonitis
6	F	26	Exploration—retroperitoneal sarcoma, cardiorespiratory failure
7	M	36	Secondary, exploratory celiotomy, hemorrhage following gastro-enterostomy performed 17 days previously
8	F	29	Salpingectomy, ectopic pregnancy, extensive preoperative hemorrhage
9	M	60	Died of intestinal obstruction before incision could be made
10	M	15	Open reduction and plating, fracture of the femur, cardiorespiratory failure
11	F	27	Cesarean section (prolonged labor with exhaustion and toxic contracture of uterus)
12	M	29	Amputation of toe (diabetic gangrene of toe with cellulitis of foot)

* Most occurred several years ago—and under straight ether. But two operating room deaths occurred in the last 3,000 operations under general anesthesia—all under cyclopropane-ether.

The advantages of spinal anesthesia, the ease with which it may be administered, the almost complete relaxation it produces and the generally satisfactory postoperative results have received widespread acceptance. However, that the method is not free of danger and, at times, is followed by serious complications, is also realized. The occasional appearance of alarming and unexpected sequelae in the human, and the easy confidence with which the procedure is condemned by certain laboratory workers, whose researches upon animals lead them to conclude that serious changes in the meninges and cord all too frequently occur, have caused the method to be the subject of severe and widespread criticism. It is with this especially in mind that the authors have reviewed their own personal experiences and have examined them in the light of what has been recently written on the dangers, complications, untoward results, *etc.*, of spinal anesthesia.

We have long known that spinal anesthesia should never be a method to

employ routinely Neither should any other single form of anesthesia, for that matter, also, we have realized, as have most surgeons, that the method is most applicable in operations below the diaphragm—better, below the level of the umbilicus—and we have appreciated that there are definite contraindications to the method and that, while there are many technics being employed, there are but one or two that are best

In evaluating the comparative safety of an anesthetic, we have no recourse but to compare it with open drop ether or gas-ether, quite universally considered the safest of all anesthetic methods This plan we have followed, especially in reference to operating room deaths, deaths in the first four days in 12-hour groups and, finally, hospital deaths

TABLE VI
RESULTS OF QUESTIONNAIRE TO POSTSPINAL PATIENTS
(1,175 Letters 911 Replies)

- (1) Have you ever had ether or gas anesthesia before having spinal?
Yes—391
No—520
- (2) If you were operated upon again, would you choose spinal?
Yes—736—80.7%
No—137—15.0%
Undecided—38

Next the question of postoperative morbidity, of hospital and posthospital complications of a temporary or permanent nature, has been considered Here one runs into a difficulty for, with the exception of certain respiratory complications which are now considered to be no less common after spinal than after inhalation anesthesia, surgeons do not commonly think of serious complications attributable to inhalation anesthesia While in the consideration of postoperative mishaps, inhalation anesthesia usually goes scot free, there have, however, been endless reports of temporary or permanent complications following the injection of various anesthetic drugs into the subarachnoid space

It is hardly fair, however, to consider inhalation anesthesia as completely free of danger The safety of open drop ether has been axiomatic—its dependability and freedom from unexpected untoward effects have rendered it proverbially a safe anesthetic equaled only by some of the newer gases, especially ethylene and cyclopropane It has, however, been disheartening to recently learn that these two anesthetics, first ethylene and now, more recently, cyclopropane, possess smoldering properties of terrifying power which are capable of being unloosed unexpectedly and with fearful and often tragic results Over 150 explosions of gas or gas-ether mixtures, 79 of which have been carefully investigated, and in which 22 persons have lost their lives, have occurred during the past few years These unfortunate occurrences have boosted the stock of other anesthetics, ether again, and with it spinal As the latter had a reputation by no means devoid of obliquity, it

has greatly needed some revivifying from the low estate into which it has sometimes fallen. The unexpected and unpredictable reactions it may produce, even resulting in sudden death from acute respiratory paralysis, and especially the late neuromuscular complications which may follow its administration have all freely been broadcast and much to its detriment.

TABLE VII

QUESTIONNAIRE TO POSTSPINAL PATIENTS

Did you ever have ether or gas anesthesia before this operation?

Yes—215

No—290

Of the 215 patients who had both spinal and general anesthesia, 154 would choose spinal were they to be operated upon for a third time, or approximately 72 per cent.

QUESTIONNAIRE TO PATIENTS HAVING AN ANESTHESIA (SPINAL)
FOR THE FIRST TIME

Would you choose spinal anesthesia if you were operated upon again?

Yes—416

Undecided—15

(depending on operation)

No—89

Of 505 patients answering questionnaire, 82.3 per cent would choose spinal for their next operation were it advisable.

We have in our own clinic, for years, been on the watch for these untoward conditions. While headaches have occurred, but with decreasing frequency, we have never seen in the hospital a single example of serious cord or meningeal injury. Foot drop, which has often been referred to as a common result of intraspinal injections, we have never seen. Neither have we ever had a patient who, before leaving the institution, has called our attention to impairment of motor function, to interference with the anal or vesicle sphincter control, to anesthetics, or paresthesias, or other evidences of definite nerve damage. We have never seen paralysis, either complete or partial, and certainly never the appearance of decubitus ulcers, retention of urine and feces or symmetric muscular atrophy, frequently referred to.

Occasionally, and usually months after the patient's discharge, either directly or otherwise, word has come to us of his complaining of persistent pain in the back, of vague numbness in the lower extremities, or, very unusually, of persistent headache. These reports have prompted further efforts toward investigating, by direct communication with the patient and, when feasible, by an office examination, to what degree actual nerve damage had occurred. Furthermore, to determine how great the incidence of late complications has been, 50 letters were sent to physicians who regularly refer the largest number of patients to us for surgical treatment, as well as 1,000 letters to patients upon whom we had operated upon under spinal anesthesia one year or more before.

It is interesting to note that in following the patients who reported postoperative complaints, most were found to have symptoms in no manner related to the anesthetic. For example, one patient emphatically denounced spinal anesthesia because of numbness in her legs and progressive loss of motor function in the lower extremities. The patient had had a plastic operation performed for cystocele and rectocele under spinal anesthesia. Some months later, she reentered the hospital complaining of the loss of strength and leg weakness, firmly believing it to be due to spinal anesthetic. Subsequent studies showed that she had rapidly progressing pernicious anemia with associated cord changes. However, this patient is not convinced that it was not the spinal that accounted for her trouble and, as her story has become well known, it is rare that a patient comes from her community but refuses to have spinal administered. Similar situations have arisen in other communities where spinal anesthesia has become widely condemned because of postoperative complications, imagined or otherwise, and yet in no possible way the result of the procedure. One patient, who has an advanced chronic polyarthritis, attributes her trouble to a spinal anesthetic administered some years ago, while still another, returning for examination in answer to our questionnaire and complaining of pain in her legs, was found to have cardiac decompensation with edema and extensive phlebitis.

In reviewing the literature dealing with postspinal injection complications, we have been impressed by the fact that in many instances, if not in the majority, untoward effects have appeared following the injection of drugs administered in combination, and that the complications seem to be of a lower incidence when procaine alone has been used. We are not convinced of the utility or safety of injecting with the anesthetic, strychnine, alcohol, starch or any of a dozen accessory substances so frequently hailed as valuable adjuncts.

We are amazed at the high incidence of serious postoperative effects which have been referred to by certain surgeons who have been led, from their unfortunate experiences, to urge that spinal anesthesia be restricted to a special group of patients or, perhaps, never to be used at all. We would long since have turned away from spinal anesthesia had we, if but occasionally, had the harrowing experience of seeing our patients develop meningitis, "aseptic" or otherwise, cauda equina neuritis, transverse myelitis, or lumbar radiculitis, as mentioned by Block and his associates.

It is probably true that many writers, particularly those speaking in enthusiastic advocacy of spinal, frequently are unaware of and, therefore, omit reference to nervous system injury, yet we repeat that with an open-minded approach to the subject and after a careful watch over a period of many years, we have not discovered prominent or even mild complications in our patients which would lead us to consider spinal a procedure possessing dangers outnumbering those commonly ascribed to other popular forms of anesthesia.

Toxic myelopathy, extensive destruction of the myelin sheath, axis-cylinders and glia, mostly at the periphery of the cord and at the zones of en-

trance of the posterior roots, have been the chief findings at postmortem examinations of patients dying from cord lesions (Brock), following subarachnoid injection of cocaine derivatives. Changes in the ganglion cells of the anterior and lateral horns have been found in toxic and experimental myelopathy induced by various spinal anesthetics.

No doubt, if it were possible for every patient, during the postoperative course, to have a careful neurologic examination by an unbiased and skilled examiner, much evidence, not obvious to the surgeon, indicating at least transitory irritation of the cord or its membranes would be discovered in every clinic where spinal is used. And this applies to our own. Nevertheless, in its daily use over a period of ten years in thousands of cases we do not recall a single incident in which the patient complained of symptoms of any consequence and which could be blamed on the method, or do we recall any patient whose convalescence was prolonged by a postspinal complication.

Of 515 consecutive patients having had spinal, who replied to a questionnaire, 130 had transitory headaches, while 375 had none. Of the 130 having had it, 69, or 53 per cent, were subject to it anyway. One hundred thirty-seven reported they experienced some postoperative numbness or pain, while 368 experienced no such discomfort whatever. Of the 137 having trouble, 66 experienced it but a few hours. Of the 137, 74 stated they would choose spinal if they had to be operated upon again. To the question "Did you have any other unpleasant reactions?" 70 replied yes, while 435 replied in the negative. Of the 70, 54 mentioned as their chief complaint backache of varying degrees and remaining present for from one week to several months. The majority, complaining of backache, stated that the pain occurred near the surface and at the point where the needle had been inserted. Of the relatively few patients who reported remote complaints, more, by far, referred to backache than to any other symptom.

Among the 5,000 consecutive operations under spinal, all performed below the diaphragm, there have been three deaths in the operating room, one in the first 2,000 and two in the remaining 3,000.

Of the two patients dying in the latter 3,000, one was a male, age 59, operated upon for a ruptured, carcinomatous ulcer of the pylorus, with peritonitis, who died 15 minutes following the administration of 120 mg of neocaine. No autopsy was obtained.

The second was a male, age 34, who died 30 minutes following the administration of 200 mg of novocain, the operation being an exploratory celiotomy for gastric ulcer. Autopsy revealed a chronic myocarditis and chronic endocarditis with aortic stenosis, cardiac hypertrophy with dilatation. From the pathologist's findings it was obvious that the patient might have as promptly succumbed under a general anesthetic.

While among our last 3,000 patients operated upon under spinal, there were two deaths in the operating room, at the same time, with a consecutive series of 3,000 patients operated upon for lesions below the diaphragm, and under general anesthesia, there were also two operating room deaths.

A questionnaire was sent to the 50 doctors who refer us the greatest number of patients. Thirty-six responded, 31 of whom stated that they have had no complaints from their patients. Five doctors returned the questionnaire giving the names of six patients who had postoperative symptoms. Five of these have been examined with the following results:

One, who complained of pain in her left leg, has chronic phlebitis.

One, who complained of headache for two weeks after operation and which cleared up spontaneously.

One, who complained of girdle pain, has developed a small recurrent incisional hernia. She weighs 250 pounds, is definitely hypothyroid and is being treated.

One complained of pain and weakness in her ankles. These have been swelling for eight years. She has shortness of breath. On examination she was found to have a systolic murmur, marked varicose veins, and pitting edema of both ankles. She was placed on medical treatment and her symptoms are improving.

One, a woman, age 48, complained of severe girdle pains and pains in her extremities. Check-up examination showed her to be suffering from a chronic polyarthritis with marked deformities of all the joints of her hands and feet. Roentgenologic examination revealed marked spondylitis of the lumbar vertebrae.

All of these patients from whom complaints were received were women, well beyond middle age. In all instances, we found that spinal anesthesia had nothing whatever to do with their present symptoms.

CONCLUSIONS

(1) Spinal anesthesia, as a method of rendering insensibility of pain, is of the very greatest utility.

(2) It is a safe procedure, as anesthetics go, and when measured in a comparative study of 10,000 operations performed by the same surgeon, was found to equal the safety of general.

(3) The likelihood of operating room deaths is no greater with spinal than with general anesthesia.

(4) With proper technic, the likelihood of serious nerve and meningeal damage is infinitesimal.

(5) Most abdominal operations are greatly facilitated by this method. For certain ones, it is almost impossible to operate without it.

(6) In many operations extensive trauma under general anesthesia is inevitable. In such instances the risk of spinal, if any exists, is more than offset by the decreased risk resulting from the lessened visceral trauma made possible by the more complete relaxation.

(7) Spinal is a procedure against which there has been a great deal of criticism, based largely upon bad results following poor selection of patients, and, especially, following improper technic. The method is one not for routine application and, when used, must be *skillfully* administered.

(8) It is quite probable that other drugs of lesser toxicity, and of even greater potency, will yet be synthesized, ultimately rendering spinal anesthesia, especially in major surgical operations below the diaphragm, the most generally satisfactory, indeed the safest, of all known forms of anesthesia. Indeed, it is not far from that status now.

REFERENCES

- ¹ Anderson, E. L. Case of Trophoneurotic Gangrene of Extremity Following Spinal Anesthesia. *Journal-Lancet*, **55**, 800-802, 1935.
- ² Brock, S., Bell, A., and Davison, C. Nervous Complications Following Spinal Anesthesia, a Clinical Study of 7 Cases, with Tissue Study in One Instance. *J A M A*, **106**, 441-447, 1936.
- ³ Davis, L., *et al*. Effects of Spinal Anesthetics On the Spinal Cord and Its Membranes, An Experimental Study. *J A M A*, **97**, 1781-1785, 1931.
- ⁴ Falk, H. C. Deaths from Spinal Anesthesia. *Am J Surg*, **11**, 461-468, 1931.
- ⁵ Foss, H. L., and Schwalm, L. J. Relative Merits of Spinal and Ether Anesthesia. *J A M A*, **101**, 1711-1716, 1933.
- ⁶ Harrison, P. W. Postanesthetic Headache. *Arch Surg*, **32**, 99-108, 1936.
- ⁷ Hyslop, G. H. Spinal Anesthesia, Nervous System Sequelae. *Surg, Gynec and Obstet*, **57**, 799-802, 1933.
- ⁸ Kelman, Harold, and Abbott, G. A. Toxic Myelopathy (Spinocaine). *ANNALS OF SURGERY*, **108**, 1001-1011, December, 1938.
- ⁹ Koster, H., Kasman, L. P., and Shapiro, A. Headache After Spinal Anesthesia. *Arch Surg*, **35**, 148-154, 1937.
- ¹⁰ Koster, H., and Wentraub, M. Complications of Spinal Anesthesia. *Am J Surg*, **8**, 1165-1179, 1930.
- ¹¹ Lindemulder, F. G. Spinal Anesthesia, Its Effect On the Central Nervous System. *J A M A*, **99**, 210-212, 1932.
- ¹² Lindemulder, F. G. Complications of Spinal Anesthesia. *Am Med*, **38**, 169, 1931.
- ¹³ Loeser, H. L. Peripheral Neuritis as a Sequela of Spinal Anesthesia. *J A M A*, **101**, 31-32, 1933.
- ¹⁴ Rygh, E. A., and Bessesen, D. H. Cause of Death from Spinal Anesthesia. *Minnesota Med*, **11**, 744-747, 1928.
- ¹⁵ Sise, L. F. Spinal Anesthesia Fatalities and Their Prevention. *New England J Med*, **200**, 1071-1074, 1929.
- ¹⁶ Smith, W. A. Neurologic Hazards of Spinal Anesthesia. *J M A Georgia*, **22**, 297-303, 1933.
- ¹⁷ Spielmeyer, W. Veränderungen des Nervensystems nach Stovainanesthetie. *Munchen med Wchnschr*, **55**, 1629-1634, 1908.
- ¹⁸ Thompson, K. W. Fatalities From Spinal Anesthesia. *Anesth and Analg*, **13**, 75-79, 1934.
- ¹⁹ Van Lier, E. H. B. Suppuration at Site of Lumbar Puncture. (Abst.) *J A M A*, **59**, 1414, 1912.
- ²⁰ Veal, J. R., and Van Werden, B. D. Mortality of Spinal Analgesia, Based on an Analysis of 30 Immediate Fatalities in a Series of 33,811 Cases. *Am J Surg*, **34**, 606-610, 1936.
- ²¹ Wossidlo, E. Experimentelle Untersuchungen über Veränderungen der Nissl'schen Granula bei der Lumbalanästhetie. *Arch f klin Chir*, **86**, 1017-1053, 1908.

SPINAL ANESTHESIA IN ABDOMINAL SURGERY*

ROSCOE R. GRAHAM, M B, AND W. EASSON BROWN, M B

TORONTO, CANADA

SPINAL ANESTHESIA has been developed to a degree which has proved its usefulness. The conflicting opinions expressed regarding this means of inducing anesthesia seem irreconcilable. The fact that such a variety of anesthetic drugs is employed indicates either the inadequacy of these drugs, or an incorrect method of administration. The undesirable sequelae reported would seem sufficient to utterly condemn the procedure. The amount of scientific nonsense which has been broadcast in respect to spinal anesthesia is amazing. On careful enquiry, many statements condemning the procedure are based on hearsay unsupported by scientific facts. An analysis of many of the reported shortcomings will reveal the fact that the anesthetic was not administered and supervised by a competent anesthetist. We cannot too strongly condemn the surgeon who gives his own spinal anesthetic and leaves the supervision of the anesthesia to an indifferent associate.

A death during or immediately following an ether anesthesia, because of the supposed safety of this anesthetic agent, is accepted as inevitable, and soon forgotten. The slightest discomfort or unusual happening following an operation performed under spinal anesthesia is often attributed, unquestionably, to the spinal anesthetic, with no attempt to support such condemnation by facts.

To assess properly the value of an anesthetic agent, one must take cognizance of not only the patient's condition during the operation, but also during the convalescence. The ideal anesthetic must achieve

- (1) Safety
- (2) Freedom from discomfort during administration
- (3) Abolition of pain and muscle spasm of sufficient duration to carry out prolonged and complicated operative procedures
- (4) A state of relaxation which permits careful and accurate dissection without traumatic retraction
- (5) Freedom from postoperative sequelae

No single anesthetic agent, so far evolved, can fulfill all these conditions. Under certain conditions spinal anesthesia fulfills these requirements to a greater degree than other anesthetic agents either singly or in combination.

Where is spinal anesthesia of the greatest value? While it has been used extensively by Shenstone and Janes¹ in thoracic surgical procedures, it is in operations within the peritoneal cavity where it has contributed so much to the advantage of the patient. This is particularly true where the surgical procedure is carried out in the upper abdomen or on the colon or rectum.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

The ability to carry out a careful atraumatic operative dissection in a difficult upper abdominal lesion reflects an advantage to the patient in several ways. An adequate operation can be carried out, thus ensuring to the greatest degree freedom from future trouble. Primary healing with a minimum of wound reaction takes place. Lesions, questionably operable with inhalation anesthesia, can often be dealt with effectively. This is particularly true of a high-lying gastric ulcer or gastric cancer. Because of the ease and safety of exposure of the common bile duct with spinal anesthesia, in a study of the last 311 cases, we explored the common bile duct in 46.9 per cent, and in the cases of calculous cholecystitis removed stones from the common bile duct in 21.4 per cent. This is at variance with our experience in biliary surgery under inhalation anesthesia, when, because of technical difficulties, largely the result of inadequate exposure, exploration of the common bile duct added greatly to the operative mortality, and hence such exploration was only undertaken when it was obvious that a stone was present. The number of common duct stones that were overlooked is only now becoming apparent. Should not such increased mortality and morbidity properly be assessed as due to the inadequacy of inhalation anesthesia, rather than to the inadequacy of technical surgical skill in the face of a serious pathologic lesion? As the result of an analysis of the last 511 operations upon the biliary tract carried out under spinal anesthesia, we now may open the common duct whenever our judgment suggests such is wise, having satisfied ourselves that this procedure will not increase either the mortality or the morbidity of the operative procedure.

The gentleness with which a perforated duodenal ulcer is exposed while tying a fat graft in place to close the perforation² is of the utmost importance in decreasing the mortality from this lesion. Spinal anesthesia achieves this. Further, the vigorous respiratory efforts associated with the induction of inhalation anesthesia are a great factor in disseminating the gastroduodenal contents which have been expelled through the perforation. Spinal anesthesia eliminates this. The routine use of spinal anesthesia in patients suffering from an acute perforation of a duodenal ulcer has in no small measure contributed to the recovery of 72 out of 76 such patients consecutively admitted to and operated upon by the staff of the First Surgical Division of the Toronto General Hospital. However, such advantages avail little unless accompanied by immediate safety and an absence of disastrous sequelae.

Our observations are based on an experience with 13,136 spinal anesthetics carried out by the Anesthetic Staff of the Toronto General Hospital, between January 1, 1930, and January 1, 1939. We have also made an analysis of 1,918 cases upon which one of us has operated, in which there were 202 hospital deaths. The analysis reveals a death rate of 10.4 per cent in this group of cases operated upon under spinal anesthesia. When one realizes that included in this group are the cases of serious and advanced malignancy, as well as the cases of acute intestinal obstruction, this mor-

tality is not forbidding. The operative mortality of one of us has ranged from 11 to 64 per cent per annum over the nine-year period, averaging 41 per cent. In view of the fact that we have been carrying out, whenever possible, palliative resections in the advanced cases of gastro-intestinal malignancy during this period, it impresses us that spinal anesthesia has in no small degree contributed to this low operative mortality.

A critical analysis of the 202 deaths in patients operated on under spinal anesthesia reveals three deaths which occurred on the table and two shortly after return to the ward, which might be contributed to by the anesthetic. An analysis of these cases follows.

ANALYSIS OF FIVE PATIENTS DYING AFTER SPINAL ANESTHESIA

Case 1—H. R., male, age 52, weight 270 pounds. Operation upon biliary tract. Spinal anesthetic: Novocain crystals, 400 mg dissolved in 10 cc of spinal fluid injected at the level of lumbar IV to V at the rate of one cubic centimeter every four seconds. When peritoneal cavity was opened, respirations ceased suddenly. At autopsy, fatty degeneration of heart and liver. In absence of any other satisfactory explanation, death is attributed to the anesthetic, with the suggestion that despite his weight of 270 pounds, 400 mg of novocain crystals was probably an excessive dose.

Case 2—W. S. A., male, age 71. Perforated duodenal ulcer. Spinal anesthetic: novocain crystals, 200 mg, dissolved in nine cubic centimeters of spinal fluid, injected at the rate of one cubic centimeter every three seconds. As the abdomen was opened and the ulcer visualized, he died suddenly. No autopsy was obtained. He had previous severe cardiovascular disease, and one suspects a cardiovascular accident, but in the absence of an autopsy we must attribute death to the anesthetic.

Case 3—F. W., male, age 68. Jaundiced, stone in the common bile duct. Spinal anesthetic: Nupercaine 1 in 1,500 dilution. Eighteen cubic centimeters injected between third and fourth lumbar vertebrae, taking 15 seconds for the injection. One and one-half hours after the administration of the anesthetic, systolic pressure fell, respirations ceased. Heart continued to beat for a few minutes. Autopsy revealed massive bilateral pulmonary collapse, with no obvious explanation, hence death attributed to anesthetic.

Case 4—W. J. H., male, age 71. Abdominoperineal excision of the rectum. Spinal anesthesia: Nupercaine, 17 cc of 1 in 1,500 dilution, injected between the second and third lumbar vertebrae. On return to bed, sudden unconsciousness, cyanosed, gasping respirations, death in few minutes. We suspected a cardiovascular accident, but were unable to secure an autopsy to support this, hence attribute death to anesthetic.

Case 5—J. R., male, age 54. Recurring jejunal ulcer. Spinal anesthesia: Nupercaine, 17 cc of 1 in 1,500 dilution, injected. Was given, during the operation, a sedative in the form of two intravenous injections of sodium amytal, the first injection being three grains and the second four grains. This was followed by supplementary deep ether anesthesia. Returned to bed, but had respiratory difficulty, was cyanosed, and never regained consciousness. At autopsy, no obvious cause of death found. It is presumed that the anoxia from which he suffered during the induction of his ether anesthesia produced cerebral damage which resulted in his death.

In Case 4 it is suggested that the change to the jack-knife position for the perineal stage was a contributing factor to the patient's death. The systolic pressure fell at this time. The further change of position on returning the patient to bed was accompanied by a further disturbance of circulation. This experience has led us to carry out the second stage of an

abdominoperineal resection of the rectum with the patient in the left lateral position. This we find is accompanied by much less cardiovascular upset.

In Case 5, because of restlessness, sodium amytal was given intravenously during the operative procedure, on two occasions, a total of seven grains being administered. It was then necessary to give supplemental inhalation anesthesia. Open ether was used. This was very difficult because the heavy sedation produced depressed respiration. It is suggested that the associated anoxia produced sufficient cerebral damage to explain the fatality.

During 1938, on the University Surgical Service of the Toronto General Hospital, a careful record was kept of all the sequelae which followed upper abdominal operations. During this period many of the anesthetics were given by interns of varying ability. For this reason, in many cases where spinal anesthesia was used, relatively large bore needles of No. 19- or 20-gauge were used for the spinal puncture. The foot of the bed was not elevated when the patient was returned to the ward.

The series includes 93 operations upon the biliary tract, 49 gastric resections, 11 perforated ulcers of the stomach or duodenum and five miscellaneous operations, a total of 158 operations, 144 of which were carried out under spinal anesthesia. This most eloquently expresses the preference of the Staff for spinal anesthesia in the major upper abdominal operations. In Table I are detailed the character and incidence of the postoperative sequelae following these operations.

TABLE I

POSTOPERATIVE SEQUELAE FOLLOWING 144 SPINAL ANESTHESIAS

Pulmonary collapse, even minor degree	15 %
Pneumonia	4 %
Headache	3.7%
Urinary retention less than 24 hrs	10.1%
Urinary retention longer than 24 hrs	8.2%
Abdominal distention, even minor degree	19 %
Deaths in hospital	10.1%

The 10.1 per cent mortality in this group on the University Service is practically the same as for the same group of private patients. Of the 144 patients who were operated upon under spinal anesthesia, 14 died. A careful analysis of these deaths fails to include, in any instance, the spinal anesthetic as a contributing factor in the patient's death. The shortest interval between operation and death was three days. Eight died of peritonitis, two of pulmonary emboli, one of coronary thrombosis, two of pneumonia and one of cholangitis. There has not been a single tragedy as a sequelae. The only nerve lesion was a paresis of the left third nerve, which cleared up in less than three weeks. The anesthetic staff have no explanation of this occurrence. It was not accompanied by any other unusual occurrence. It was discovered the day following operation, and is thus attributed, rightly or wrongly, to the spinal anesthetic.

The necessity for catheterizing the patients postoperatively is more fre-

quent than after inhalation anesthesia. While the incidence of chest complications is approximately the same as after inhalation anesthesia, the serious lesions are less frequent, and fatalities from respiratory infection are infrequent. Many cases diagnosed as dying from pneumonia postoperatively are found to have a fatal peritonitis at autopsy. The aspiration of the bronchi by a urethral catheter, as advocated by John Alexander,⁴ of Ann Arbor, has proven of great advantage in the cases with pulmonary collapse. The volume of mucus which it is possible to aspirate by this procedure is surprising.

Despite these sequelae, the benefits of the anesthesia in our opinion outweigh the disadvantages, and indeed, apart from the necessity of more frequent postoperative catheterization, we believe the sequelae are no more than those following inhalation anesthesia with ether.

Why, then, is there such a conflict of opinion regarding the value of spinal anesthesia? This we believe results from two sources. First, the character of the drug used, and second, the experience of the anesthetist. The drugs used for inducing anesthesia are either (A) Isotonic with the spinal fluid (B) Heavier than the spinal fluid (C) Lighter than the spinal fluid.

When a drug is used in which the level of anesthesia is determined only by elevation or depression of the patient's toiso, we believe the factor of error and the possibility of accident are too great to warrant its use. For this reason we have never used such agents, of which spinocaine, and more recently pontocaine and glucose, are the most popular. We prefer to use as anesthetic agents those in which the height of anesthesia is determined by the volume of fluid injected into the spinal canal. The natural curve of the spinal column is utilized as a protection against respiratory paralysis which results if the anesthetic reaches the cervical region. The drugs we use are procaine and nupercaine. The former is used if the operation will be of less than one hour's duration, or in the cases where it is impossible for the patient to lie on the abdomen, as is necessary if nupercaine is used. This latter drug almost invariably will give adequate anesthesia for at least two hours. In our experience there is less fall of the systolic blood pressure with nupercaine than with procaine, although with expert supervision this disturbance may be controlled adequately in most instances.

The second factor which has led to the condemnation of spinal anesthesia is an erroneous method of administration. We cannot too strongly condemn the practice of a surgeon being his own anesthetist. The technic of administering the anesthetic is important, but of no more importance than the preparation of the patient for the anesthetic, or the intelligent supervision of the patient throughout the whole operative procedure. Spinal anesthesia is a dangerous anesthetic agent unless administered and supervised by an expert anesthetist trained in spinal anesthesia.

With the exception of the increased incidence of postoperative catheterization, the complications seen on the University Service are conspicuous by their absence. On the private side particularly, is this true of headache and

abdominal distention Headache now is a rarity following spinal anesthesia In the clean abdominal cases, postoperative distention as a complication is infrequent, much different from our experience with the same type of case when the operation was carried out under inhalation anesthesia This freedom on the private side from postoperative complications after spinal anesthesia can be due only to the fact that in each instance the patient is prepped, anesthetized and supervised by an expert medical anesthetist This we believe to be of the utmost importance, if we are to secure the greatest advantages from the use of spinal anesthesia

The following is the technic which we have come to adopt We shall discuss the four stages which we believe to be important

(A) *Selection of the Patient*—With increasing experience, we have extended the use of spinal anesthesia very greatly Emergency operations have been necessary when we felt it wise to modify our previously determined contraindications and use spinal anesthesia, and to our delight the patient benefited As a result of such experience we have gradually decreased our contraindications In the elderly patient, with severe cardiovascular disease associated with hypertension, or a history of previous vascular accidents, spinal anesthesia is given only if the disease be of a lethal character and when perfect relaxation permitting meticulous atraumatic dissection is essential to recovery We gradually are being convinced that with adequate collateral support few patients need be denied the advantages of spinal anesthesia In patients with carcinoma of the stomach or colon, adequate contraindications must be advanced to deny such patients a spinal anesthetic We believe, in diseases of such seriousness, such contraindications must be extremely rare A surgeon who operates upon a patient suffering with acute intestinal obstruction using inhalation anesthesia, if adequate facilities for spinal anesthesia are available, is guilty of malpractice In the presence of an acute intraperitoneal inflammatory lesion, such as a perforated ulcer or a perforated appendicitis, the advantages of the "still" peritoneal cavity accompanying spinal anesthesia are obvious

(B) *Preparation of the Patient*—The adequate restoration of body fluids and salts should be always assured before anesthesia This may be accomplished by the oral or intravenous administration of fluids Blood transfusion is of great help on occasions So much importance do we place on the correction of the biochemical upset, that we will defer operation for some hours, even when the diagnosis be that of a perforated duodenal ulcer To administer a spinal anesthetic to a dehydrated or exsanguinated patient, is to court disasters which cannot properly be charged to the anesthetic procedure, but to poor judgment and inadequate knowledge of the collateral disturbances which accompany such states

Adequate preoperative sedation is of the utmost importance The variable definition of "adequate" explains further conflict of opinion regarding the merits or demerits of this anesthetic procedure If we achieve for the patient a drowsiness which is accompanied by an utter disregard for the

surroundings, we believe we have adequate sedation. Anything short of this is inadequate. With inadequate sedation we have an apprehensive patient, with all the associated physiologic and biochemical phenomena. Most important from our standpoint are an acceleration of the pulse and increased respiratory rate. Nausea during the operation is very rare in the presence of adequate sedation. To achieve adequate sedation, the following medication is administered. Starting 1½ hours preoperative, we give to adult patients morphia Gr ¼, hyoscine Gr 1/200. Three-quarters of an hour preoperative, we give morphia Gr 1/6, hyoscine Gr 1/400 (in female patients morphia Gr ⅛). One hour preoperative, nembutal Gr 1½ per os—this repeated in 20 minutes if patient not dozing, and if alert on reaching the operating theater, a further Gr 1½ is repeated. This latter dose of nembutal is rarely necessary. If, after the anesthetic is administered, the patient is still wakeful or nauseated, sodium amytal is administered intravenously. If intravenous fluid is being administered, the sodium amytal is given slowly into the intravenous tubing until the patient becomes quiet. Usually about two grains will suffice and often no more is required. If after some time the patient shows signs of restlessness, further administration of approximately one grain may be administered, the patient's quietness being the criterion of dosage. If, however, the duration of the operative procedure is such that there is a possibility of supplementary inhalation anesthesia being necessary, all intravenous sedation should be withheld and inhalation anesthesia given in its place, the agent used being either nitrous oxide, cyclopropane or a combination of either with ether. The difficulty and danger of administering supplementary anesthesia with heavy sedation is too obvious to require discussion. For this reason, if supplementary anesthesia is necessary in an upper abdominal operation, we use splanchnic anesthesia and field block of the abdominal wall. The technic popularized by Finsterer, of Vienna, we have found adequate and of great advantage. By such we avoid the necessity for deep inhalation narcosis.

(C) *Technic of Administering the Anesthetic*—Before the anesthetic is administered, a hypodermic injection of Gr ¾ of ephedrin is given. The patient lies on the side with the knees drawn well up and the back bowed with the assistance of a nurse. A midline puncture of the spinal canal is made with a sharp short-beveled No. 22-gauge needle. We are convinced of the value of the small gauge needle. The level and duration of anesthesia is determined by the volume injected. With nupercaine we always use a solution of 1-1,500 dilution, and in a difficult and complicated gastric case have injected as much as 19 cc without the withdrawal of spinal fluid. The nupercaine solution is injected quite slowly, so that undue pressure will not occur in the spinal canal. The patient is then made to lie on the abdomen for eight to ten minutes. This step of course is unnecessary if procaine is used. It is of the utmost importance to make sure that with the patient lying on the abdomen, the upper thoracic curve of the spinal column is higher than the cervical region. A pillow placed under the chest while the patient

lies on the abdomen ensures this and prevents the anesthetic agent from going too high. It is quite unnecessary to tip the table. If the operation be of lesser magnitude, or if for some reason the patient cannot lie on the abdomen, procaine in crystal form is substituted for nupercaine. The maximum dose should not exceed 300 mg and is dissolved in the withdrawn spinal fluid. Twelve cubic centimeters volume will ensure anesthesia in the upper abdomen. During the operative procedure a tent is made over the patient's head by using the end of the laparotomy sheet and a stream of oxygen is run in at the rate of 60 liters per hour. Ravdin⁵ has recently supported the wisdom of this procedure. During the operation, observation of the blood pressure and pulse rate are made at five to ten minute intervals, and any tendency to a fall in the systolic blood pressure is combated by the repeated injections of small doses of epinine combined with ephedrin during the operation. Usually about three minims of epinine and Gr $\frac{1}{4}$ of ephedrin is given at one dose. This type of supervision enables the anesthetist also to anticipate the necessity for the intravenous administration of fluids before an acute emergency arises.

(D) *Postoperative Precautions*—When the patient is returned to bed, an intravenous of at least 1,500 cc of normal saline is administered by the drip method at a rate of approximately 125 cc per hour. The foot of the bed is elevated six inches for ten hours. To these two procedures, and the use of No. 22-gauge needle for introducing the anesthetic agent, goes the credit for the almost complete disappearance of "spinal headache" in the private cases. Over-breathing of the patient stimulated by the administration of carbon dioxide, together with a change in position of the patient from one side to the other every two hours for the first 24 hours after operation, does much to minimize the respiratory complications. If signs of pulmonary collapse, such as dulness on percussion and fine râles are heard, the suggestion of Dr. John Alexander⁴ to aspirate the bronchus with an urethral catheter has been of great help, and the simplicity and ease of its execution commends itself to us. If the patient has not voided in 12 to 14 hours post-operatively, an urethral catheter should be passed. This may have to be repeated, but we have had no case when this complication, if such it be, was more than a nuisance.

CONCLUSIONS

(1) The evolution of spinal anesthesia has reached a stage where the permanence of the procedure is assured.

(2) Its safety is in direct ratio to the experience of the anesthetist. It must be administered and supervised during the operation by a physician specially trained in its use.

(3) Nupercaine in dilution of 1:1,500 is the agent of choice, being replaced by procaine when conditions prevent its use.

(4) Adequate preoperative sedation is of great value during the opera-

tion in preventing nausea and the acceleration of the pulse and respiratory rate, as well as lessening the changes in the blood pressure

(5) A gross fall in the systolic blood pressure can be prevented by the hypodermic injection of Gr $\frac{3}{4}$ of ephedrin immediately before administering the anesthetic and the injection of small doses of epinine and ephedrin during the operation whenever any fall in pressure commences, further controls serious fluctuation of the systolic pressure

(6) Anoxia is prevented by a stream of oxygen run into a tent about the head, formed from the end of the laparotomy sheet

(7) The use of a small No 22-gauge needle for the spinal puncture reduces to a minimum the leak of spinal fluid from the dural puncture. The prevention of such a leak in conjunction with the intravenous administration of fluids by the drip method and elevation of the foot of the bed immediately following the operation has practically eliminated the "spinal headache"

(8) Postoperative over-breathing, stimulated by the administration of carbon dioxide, together with frequent changes in posture, minimize the incidence and seriousness of chest complications

REFERENCES

- ¹ Shenstone and Janes Canad Med Assn Jour, 38, 538, 1938
- ² Graham Perforated Ulcer Surg Gynec and Obstet, 64, 235-238, February, 1937
- ³ Gordon Personal communication
- ⁴ Alexander Address, Academy of Medicine, Toronto
- ⁵ Ravdin, I S Some Recent Advances in Surgical Therapeutics ANNALS OF SURGERY, 109, 321-333, March, 1939

FURTHER EXPERIENCES IN THE USE OF SPINAL ANESTHESIA FOR THORACOPLASTY*

FRASER B GURD, M D , A M VINEBERG, M D ,
AND WESLEY BOURNE, M D

MONTREAL, CANADA

FROM THE GRACE DART HOME HOSPITAL (FOR PULMONARY TUBERCULOSIS), MONTREAL, CANADA

IN JUNE, 1937, a paper¹ describing our experiences in the employment of spinal anesthesia for thoracoplasty was read before the American Association for Thoracic Surgery. At that time, we reported that, commencing in July, 1936, we had operated upon nine patients and performed 17 operations for thoracoplasty under spinal anesthesia. We now feel it advisable to report our experiences since that date.

Sixty-seven cases of extrapleural thoracoplasty (including five cases of extrapleural pneumothorax induction) have been operated upon at the Grace Dart Home Hospital since 1934. The clinic is not a large one, and during the two years from July, 1934, to July, 1936, 27 cases have been operated upon, employing during this period different forms of anesthesia. In this way we used avertin and nembutal as preliminary sedation or basal anesthesia, local novocain infiltration and nerve blocking, nitrous oxide and oxygen (with or without ether), cyclopropane and intravenous evipal. In consequence, we believe, of the rather unusual nature of cases submitted to us for operative interference, our death rate was high and the number of bronchogenic spreads was, also, high.

Of the first 27 cases, 15 of which showed bilateral active disease, two died soon after operation, one on the seventeenth day from hemorrhage, and four within six weeks of the time of operation as the result of spread of the disease and the onset of acute pneumonic phthisis. There were altogether during this period eight cases in which more or less massive spread of the disease occurred.

The results of operative interference in the early group of cases operated upon in our institution was such that we were depressed and disappointed. It seemed that, especially for the type of case presenting itself at our clinic, inhalation anesthesia was too likely to be followed by unfavorable sequelae to justify the continuation of such anesthesia unless a substitute was not available. Despite the absence of favorable reports from other clinics regarding the use of high spinal anesthesia, we felt that were it possible to carry out such a procedure with relative safety during the operative period the patients might and should be better in so far as postoperative unfavorable sequelae were concerned. As Shields² had previously stated "In the presence of

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

pulmonary tuberculosis spinal anesthesia would be chosen by many should they be faced with an abdominal operation"

Commencing, therefore, in the summer of 1936, we have employed, routinely, spinal anesthesia for performance of extrapleural thoracoplasty and the induction of extrapleural pneumothorax. Spinal anesthesia has been employed for all first and second stages and, in many cases for the third and fourth stages—if the latter have been required.

In this way we have operated upon 42 cases. Twenty-four have shown active bilateral disease and eight were cases of tuberculous empyema. There have been two deaths in the operating room. In addition, we have had three disturbing experiences in the operating room. All three of these cases were similar, and the report of the case exhibiting the most severe reaction is presented in some detail. There have been three slight spreads or reactivations, in all three of these, however, the condition has promptly subsided. Apart from the two deaths in the operating room, we have had no deaths within two months from the date of operation.

Case Report—Hosp No 3234, G P, female, age 19, married, was admitted to the Grace Dart Home Hospital, September 14, 1937, with a history of onset of disease two years previously. At time of admission, patient had history of cough, marked loss of weight, blood-streaked sputum, slight infiltration right apex, and active disease involving upper third of left lung. Sputum was negative. She left hospital against advice and was readmitted September 13, 1938, at which time there was an incomplete pneumothorax on the left side. The upper two-thirds of the left lung showed active disease with an adherent apex which had failed to collapse under pneumothorax. The right side appeared stationary.

Operation—September 28, 1938. A left-side extrapleural pneumothorax was attempted under spinal anesthesia. Approximately four inches of the fourth rib were resected and separation of the parietal pleura from the endothoracic fascia was accomplished. When the procedure was all but finished, patient stopped breathing and within a very few seconds the heart stopped beating.

A sterile towel was rapidly plugged into the wound and the patient turned on to her back. One cubic centimeter of adrenalin was then injected into the heart through the fourth interspace, just to the right of the sternum. The heart commenced to beat within a few seconds after the adrenalin injection. Artificial respiration was carried out, approximately four minutes later the respiratory rate returned to normal, within ten minutes the blood pressure was sufficiently high and the heart sufficiently strong for the operator to continue the surgical procedure. It is important to note that as soon as respiratory and cardiac failure occurred the patient was placed in the Trendelenberg position.

First hour postoperative. Respirations were shallow. There were spasms involving arms, head and neck. These spasms lasted a few seconds and occurred approximately every half hour. They were associated with crying and screaming spells. The following day, the spasms continued with decreasing frequency and, approximately 12 hours after the incident had occurred, the patient was able to understand spoken words but was unable to speak intelligently. She was cooperative but was unable to remember events immediately preceding the operation and had no memory of daily events. Within one week her memory for current events returned to normal, although there was no return of memory concerning events that occurred four days prior to operation. She was transferred October 20, 22 days after her operation, to a convalescent institution, at which time her mentality was normal and her wound well healed.

Of the 42 cases in the spinal group, there were 37 thoracoplasties and five inductions of extrapleural pneumothorax. In all, 99 operations have been carried out under spinal, and 12 under local anesthesia.

As previously reported, Etherington-Wilson's³ technic, as described by him before the Royal Society of Medicine in London, in 1933, has been employed with the modifications as described by Bourne and O'Shaughnessy,⁴ in 1936.

The technic employed at present is as follows. The patient is supported sitting upright by assistants. Nupercaine in 1:1500 solution is employed for anesthesia. The needle is introduced between the second and third lumbar spines and from 12 to 13 cc are introduced somewhat slowly without barbotage. From the commencement of the time of injection a stop-watch is started and time allowed for the passage of the solution upward.

Although it would perhaps be more scientific were we able to state the exact number of seconds during which the solution is allowed to rise in the spinal canal, based upon the length of the patient's back, in centimeters, we have, hitherto, simply noted the patient's back to be either long, short or medium. The length of time allowed for the rise of the solution has been as a rule from 50 to 55 seconds with an absolute maximum of 60 to 65 seconds. It is of assistance to the anesthetist if the time is called off by an assistant at five second intervals. As soon as the length of time previously decided upon has been reached the patient is immediately laid down with the head and upper part of the torso inclined at an angle of about 20° downward from the flat.

As previously reported, it is believed that

(1) Ten cubic centimeters of nupercaine solution (1:1500), 20 to 25 seconds, anesthetizes the first lumbar nerve segments—suitable for operations upon the lower limbs and the perineum.

(2) Twelve cubic centimeters of nupercaine solution (1:1500), 30 to 35 seconds, anesthetizes the tenth thoracic segments—suitable for operations upon the lower abdomen and pelvis.

(3) Fifteen cubic centimeters of nupercaine solution (1:1500), 40 to 45 seconds, anesthetizes a high zone, fifth thoracic segments—suitable for operations upon the upper abdomen and lower thorax.

As the result of our continued experiences since our first publication, we wish to modify the statement made with regard to the amount of material to be injected. We now believe that 15 to 17 cc of nupercaine solution is too large and have come to the conclusion that 12 to 13 cc is both adequate and accompanied by a greater measure of safety. It would seem from our experiences that 12 to 13 cc of 1:1500 nupercaine solution, allowed to rise for 50 to 55 seconds in all but the longest backs, suffices to affect the lower cervical segments and so render anesthesia complete for the removal of the first rib and apicolysis in accordance with Semb's recommendation.

Although, hitherto, we have not attempted to estimate the specific gravity of the cerebral fluid, this, as is well known, varies somewhat. It is usual for

the specific gravity of the cerebral spinal fluid to be 1 007, although it is sometimes higher. Since the specific gravity of the nupercaine solution used is 1 003, and since we are dependent upon the difference in specific gravity of the two solutions for the height to which the anesthetic solution will rise in a given length of time, we propose in the future determining the specific gravity of the cerebral spinal fluid and intend to use for this purpose Babour's⁵ falling-drop method.

We have continued to use the preoperative medication substantially as recommended in our previous contribution. Ninety minutes before operation the patient receives morphine, Gr $\frac{1}{4}$ and hyoscin, Gr $\frac{1}{100}$, subcutaneously. Twenty minutes before operation the patient's condition is checked, and if, as is usually the case, he, or she, is not sound asleep the same dose is repeated. In consequence of this rather heavy sedation the patients are uninterested during the induction of the anesthesia and have a substantially complete amnesia regarding their experiences in the operating room. At the same time, almost immediately following operation, it is possible to wake them up and to obtain cooperation in the sense of ingestion of fluids and purposeful deep breathing and coughing. We believe that with increased doses of the two drugs mentioned nausea is less likely to occur and that there is less shock. We have not continued the use of atropine.

Since we are of the opinion that the two deaths which occurred in the operating room were due to the systemic effects, especially with reference to vasomotor reaction, and not to the effect of the anesthesia within the spinal canal, we have become more willing to employ analeptics early during the period of anesthesia. In any event, it must be stated that if analeptics, as for instance ephedrine, are to be withheld until such time as they are proven to be necessary, the care with which the patient is watched must be faultless. When analeptics are withheld until required, and it may be said that this is our usual procedure, ephedrine and the pressor principle of the posterior pituitary are administered intravenously and together. The dose of these two drugs is ephedrine 0.5 cc ($\frac{3}{4}$ Gr), pitressin 0.5 cc.

At the completion of the operation strychnine Gr $\frac{1}{30}$ is administered and repeated every three hours for three doses. This procedure has been carried out, in accordance with the teachings of Yandell Henderson,⁶ for its effect upon skeletal muscle. Immediately upon return to the ward, patients have received 1,000 cc of 5 per cent glucose in saline solution to which 10 units of old (unmodified)⁷ insulin have been added. In but two cases has it seemed advisable to employ transfusions postoperatively, both of these cases had been suffering from massive pulmonary hemorrhage prior to operation.

Upon return to the ward, the patients have been allowed to sit up and their cooperation asked for. There has been early return of appetite, so that in this respect, at least, the depressing effect of operation has been in large measure overcome. Postoperative headache has been consistently absent.

In our earlier contribution we tabulated the advantages and disadvantages of spinal anesthesia for extrapleural thoracoplasty. With further experience

in the employment of the method, we copy with but few modifications the memoranda from our first paper

(1) The patient does not lose consciousness, although under the conditions of premedication which we employ sleep is induced and a substantially complete amnesia follows

(2) It is possible to induce the patient to cough, upon instruction. The respiratory effort, particularly if oxygen be administered, is as quiet as may be expected by any form of anesthesia

(3) Owing, presumably chiefly, to the drop in blood pressure and the quiet, tranquil respiratory effort, there is less bleeding, we believe, during the course of the operation, at the same time we have not noted any tendency, whatever, toward postoperative hematoma accumulation

(4) In consequence of the quietness of the chest wall and the complete muscle relaxation—of special importance in removal of the transverse processes—and the smaller amount of bleeding, operation can be performed more easily and more expeditiously, therefore, more safely

(5) On return to the ward, cooperation on the part of the patient can be obtained at once, particularly in the sense of deep breathing and purposeful coughing

(6) Although we have made a practice of administering strychnine, and 750 to 1,000 cc of 5 per cent glucose in normal saline, to which 10 units of insulin have been added, as a routine in all cases immediately upon return to the ward, this has not been done on account of shock phenomena being exhibited

(7) Patients have been able to commence the ingestion of nourishment within two or three hours after operation, in all cases, and have been able to return to full diet with the lapse of a very much shorter period of relative starvation than in cases in which other anesthetics have been used

(8) The induction period, after the patient arrives in the operating room, is a short and simple procedure

Objections—(1) Although the patients do not suffer pain, a few have grunted when traction on the ribs has been made. Using scopolamine and morphine, patients have difficulty in remembering such an incident on the day following operation

(2) There would appear to be a risk of involvement of the phrenic roots, such interference with functioning of the diaphragm has not been noted in any of our cases presumably because the anesthetic is so dilute when it reaches the midcervical region that motor function is not completely destroyed. Should such an accident develop, it would seem probable that serious results might well be avoided by the employment of artificial respiration or intra-tracheal insufflation

(3) In our previous communication, we note that the possibility of severe circulatory disturbance must be considered, although at that time we had had no disturbing experience. As noted in this paper two patients have died and three others suffered important circulatory failure. Since we believe

SPINAL ANESTHESIA FOR THORACOPLASTY

that prompt administration of stimulants to the cardiac system is capable of correcting such failure, it becomes of special importance in such cases that more than usual caution on the part of the anesthetist in the observation of his patient is imperative

REFERENCES

- ¹ Gurd, Fraser B, Vineberg, A M, and Bourne, Wesley Our Experiences in the Employment of Spinal Anesthesia for Thoracoplasty Jour Thoracic Surg, 7, No 5, 506-511, 1938
- ² Shields, H J Spinal Anesthesia in Thoracic Surgery Can Med Assn Jour, 29, 528, 1933, Anesth and Analg, 14, 193, 1935
- ³ Etherington-Wilson, W Intrathecal Nerve Root Block Some Contributions and a New Technique Proc Roy Soc Med, 27, (Pt I), 323, 1933-1934, Brit Jour Anæsth, 9, 43, 1934, Anesth and Analg, 14, 102, 1935
- ⁴ Bourne, Wesley, and O'Shaughnessy, P E The Etherington-Wilson Technique in Intrathecal Segmental Analgesia Canad Med Assn Jour, 35, 536, 1936
- ⁵ Barbour, H G, and Hamilton, W F The Falling-Drop Method for Determining Specific Gravity J A M A, 88, 91-94, 1927
- ⁶ Henderson, Yandell Atelectasis, Massive Collapse and Related Postoperative Conditions Bull New York Acad Med, 2nd Series, 11, 639, 1935
- ⁷ Gurd, Fraser B Postoperative Use of Insulin in the Nondiabetic with Special Reference to Wound Healing ANNALS OF SURGERY, 106, 761-769, 1937

INTRAVENOUS AND REGIONAL ANESTHESIA*

JOHN S LUNDY, M D

SECTION ON ANESTHESIA, THE MAYO CLINIC

ROCHESTER, MINN

I APPRECIATE this opportunity to take a short part in this symposium on anesthesia, and believe that your choice of the subject of anesthesia for the symposium is significant of the development of anesthetic agents and methods during the last decade. I would like to mention briefly some of my own experiences in and reactions to this development.

The change from the scanty equipment necessary for the use of volatile anesthetics occurred as more and more complicated mechanisms were devised for the use of gaseous agents alone or in combination with volatile agents. At the moment, the modern gas machine is an expensive piece of equipment and is relatively complicated, but its economy and efficiency of operation have justified its high cost. It serves as a device for the administration of oxygen and combinations of oxygen and carbon dioxide and of oxygen and helium, as well as for the purpose of producing anesthesia. Artificial respiration is effectively carried out by intermittent compression of the breathing bag for the insufflation of oxygen. The skillful use of such a machine requires considerable instruction and practice on the part of the anesthetist, and further improvement may be looked for in these machines. This will be necessary, because of the inherent dangers associated with the use of inflammable and explosive anesthetics and the need for control of this hazard.

The introduction of such an agent as triethylmethyl alcohol (avertin) has greatly increased the usefulness of the rectal method of anesthesia. Other agents have been tried, and this method has yet to have its greatest day of usefulness. Local and regional methods of anesthesia have had alternate periods of popularity and unpopularity. Factors that have influenced this have been the periodic introduction of promising agents and of modifications of technic that have increased the safety and satisfaction with which the methods were used. The intravenous method of anesthesia has slowly developed into a useful method.

The field of anesthesia has gradually broadened so that the limits of usefulness of the anesthetist rest largely on his willingness to apply himself. In the preoperative period he has been useful as a member of the surgical team in preparing the patient for anesthesia and for operation. During anesthesia, because the surgeon and his assistant are fully occupied with the technical steps of the operation, the anesthetist has been the most readily available person to carry out whatever measures are necessary to support the patient, for example, transfusion of blood or in the intravenous administration of

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

solutions of acacia or other fluids. There has been a striking change in the method with which such treatment may be carried out. Previously some one of the surgical team would cut down on a vein and administer the solution. The confusion in connection with this procedure varied with the frequency with which it was carried out and the excellence of the team work exhibited. To-day, the anesthetist is ready to insert a 15 gauge needle, which contains a stylet, into a vein just as soon as anesthesia has been induced and just prior to the beginning of the operation. The point at which the veins are usually well filled with blood is most readily available for venipuncture. If during the course of operation, there is need for blood or fluids, there is no confusion or delay in withdrawing the stylet from the needle and permitting the solution to enter the vein. The large gauge of the needle permits the very rapid introduction of large quantities of solution, and at the same time the flow can be regulated by a pinchcock. Because of the anesthetist's experience with the use of the laryngoscope and the introduction of the intratracheal tube, he has learned to clean the respiratory passages, at the end of the operation, by means of an aspirating catheter. A few anesthetists have had training in the use of the bronchoscope and are of invaluable service in the postoperative period in the event that postoperative bronchoscopy is needed for relief of collapse of a lung. The supportive treatment of the patient in the postoperative period, in the event that such measures are necessary, may be carried out by the anesthetist.

The ready availability of the anesthetist in the hospital has been a factor in his usefulness as a supervisor in cases in which oxygen therapy and prolonged artificial respiration are required. This is particularly advantageous in obstetric practice when the newborn infant may need assistance to establish adequate pulmonary ventilation. The study of analeptic and supportive drugs has been impressed upon the anesthetist. For those patients who suffer intractable pain the anesthetist has collaborated with the attending physician in the control of such conditions. He has found a use for his methods of regional anesthesia as diagnostic procedures and as therapeutic procedures in certain cases.

The frequency with which he has been carrying out venipuncture has very naturally made skillful venipuncture available to hospitalized patients generally, and is particularly appreciated by those patients in whom this is ordinarily very difficult. Perhaps intravenous administration of fluids and drugs has been employed for a long time in a given case and most of the veins are thrombosed and are not usable. Even in these cases, venipuncture may be easily carried out by the proper application of heat and by the use of warm antiseptic solution, local anesthesia, a properly selected sharp needle, and utilization of tourniquet not only to dilate the vessel but also to anchor it so that it may be put on the stretch and easily entered with the needle. A knowledge of the situation of readily available veins in the body comes to the experienced individual and is of advantage to the patient, for example, the most readily available vein in the child who is one year of age is often

in the back of the hand and wrist, or it may be the saphenous vein near the internal malleolus

These illustrations of the functions that the anesthetist can carry out call to mind the bright hope for the future development of this branch of medicine. A sign¹ of what may be expected in the future has been the recent approval of the American Board of Anesthesiology, Inc., an affiliate of the American Board of Surgery, by the Council on Medical Education of the American Medical Association. It is a genuine satisfaction to see the eagerness with which the requirements of this Board are being met, and the stimulus it is to many of those who have perhaps not kept up with modern trends as well as they might have. I anticipate that beneficial results will appear from the studies carried out by the various candidates who wish to prepare themselves for examination by the Board.

It seems to me unnecessary to stress the technical means of blocking the various nerves. Not much of skill in one's fingers can be transmitted by word of mouth. I am limiting my remarks purposely to some of the points that I have been asked to consider.

Intravenous Anesthesia—The intravenous method of anesthesia is the newest and probably the most interesting method at our disposal. The method was begun in 1872, when Oie, of Lyons, used chloral hydrate. Since that time other drugs such as hedonal (methyl-propyl-carbinol-urethane), ipral (calcium ethylisopropylbarbiturate), alcohol in physiologic saline solution, ether in physiologic saline solution, sodium amytal, pentobarbital sodium (nembutal) and many other barbiturates have been used. Most of these drugs are no longer used in intravenous anesthesia. At this time, evipal (n-methylcyclohexamyl methyl barbituric acid) and pentothal sodium (sodium ethyl 1-methyl butyl thiobarbituric acid) are the drugs that are most frequently used for this purpose. The German product evipal (evipan) is available throughout the world, pentothal sodium has been available principally in the United States and the British Empire. The outstanding chemical difference between evipal and pentothal sodium is that the latter contains sulphur and evipal does not. This is of increasing importance, since it has been noted that persons who have been prepared for operation by the use of sulfanilamide should not be given pentothal sodium until a day has passed since the last sulfanilamide was taken. Damage to the liver by sulphur, with resultant jaundice and general malaise, has been noted in such instances. In such cases evipal in 2.5 per cent solution may be used, one must bear in mind this particular difference in the two agents.

For some time, it was advised that preliminary medication should not be employed prior to the use of intravenous anesthesia with either evipal or pentothal sodium. I think it is safe to say that the general consensus now is that preliminary medication should be used. It does reduce the amount of the anesthetic agent necessary to produce anesthesia, and the recovery period is shorter and the patient is more quiet. The journey to the operating room is less annoying to the patient. It is safer to use preliminary medication with

a barbiturate than it is to use a large amount of the barbiturate alone to produce anesthesia. There is, in general, a class of operations, such as removal of a single tooth, removal of packs, lumbar puncture and operations in which the pain must be abolished for only five minutes or less, in which no preliminary medication is necessary.

The use of intravenous anesthetics should entail the use of as dilute a solution as can be used effectively. Pentothal sodium at first was used in a 10 per cent concentration, but the site of injection became sore and painful if any of the solution was injected extravascularly. A 5 per cent solution was substituted and apparently was just as satisfactory as the 10 per cent solution in the induction of anesthesia, but once in about 1,000 cases a phlebitis would develop one to three weeks after operation and would last for two weeks to three months. For this reason, I substituted a 2.5 per cent solution for the 5 per cent solution. I now prefer this mixture instead of the 5 per cent or 10 per cent solution as it induces anesthesia more slowly and more safely. The patient does not complain of the induction being so sudden as when a 5 or 10 per cent solution is used. The incidence of phlebitis has been reduced to about one in 3,000 cases. Two interesting cases illustrate the less irritating properties of the 2.5 per cent solution as compared with the 5 per cent concentration. In one case, a 5 per cent solution of pentothal sodium was injected intra-arterially and the patient complained of an intense smarting sensation in the hand during induction of anesthesia. At a later date a 2.5 per cent solution was injected intra-arterially and the patient complained of only a little discomfort in the hand before anesthesia appeared. Intra-arterial injection should be avoided.

I will now refer to another change in technique in the use of evipal and pentothal. It was common practice to inject a dose sufficient to anesthetize the patient and then immediately to inject a second dose equal to that which was sufficient to induce anesthesia. The needle then was removed and the operation carried out under whatever anesthesia occurred as a result of the dose administered. The next improvement in technique was to use the intermittent method of injecting the solution, that is, to maintain the point of the needle within the lumen of the vein, and, after anesthesia had been induced, to inject small amounts as necessary to maintain anesthesia. This technique was similar to the administration of ether by the open drop method, the agent was applied when and in such doses as were needed. This technique allowed the drug to be used for very much longer operations than did the earlier technique, which consisted of one or two injections.

However, since the patient was inhaling only air, it was found necessary to keep the respiratory passages patent continuously, as the effort to breathe was not vigorous. A paper or the use of a cotton "butterfly" over the nose was considered a help in recognizing that definite exchange of air was taking place, and this is still useful. It was decided that this type of anesthesia should not be used for children because of the smallness of the respiratory passages and because pulmonary ventilation often was inadequate when only air was

breathed. In certain cases in which respiratory depression became prolonged and anoxemia was evident, it was found advisable to carry on artificial respiration by using oxygen from the anesthetist's gas machine. It soon was noted that if the oxygen was administered throughout the period of intravenous administration of the anesthetic agent, respiration was more vigorous and the effectiveness of the pulmonary ventilation could be noted by watching the respiratory exchange as the bag emptied and filled. The administration of oxygen also tended to improve the color of the patient. This was particularly true in cases in which there was cardiac disease and no period of anoxemia could be permitted. These patients did very well during the period of anesthesia and it can now be said that the safest technic is to administer oxygen to these patients as soon as anesthesia has been induced and until they begin to show signs of recovery. When this technic is used, the amount of the barbiturate which may be administered can be greatly increased and more profound anesthesia and relaxation can be secured. As a result of applying this technic of intravenous anesthesia, the method has been extended in some places in major abdominal operations and to its use in cases in which the patients are small children. The technic now used may be said to be at this point of development, but within the year one may expect to see further advances. In time, as new drugs are introduced and more experience is gained with the method, many of the problems of anesthesia no doubt may be solved. *A good illustration of one problem in anesthesia is the elimination of the hazard associated with the use of inflammable and explosive inhalation anesthetic agents.*

One of the most promising modifications that we have employed recently at the clinic is the use of pentothal sodium in inducing anesthesia prior to using inhalation anesthetics, especially in cases in which the patients are hypertensive individuals who have almost always resisted the induction of anesthesia, who often have had exaggerated stages of excitement during induction and who also have had periods of extreme cyanosis which are undesirable in the presence of high blood pressure. These patients usually respond very nicely to an intravenous injection of pentothal sodium, 3 or 4 cc and never more than 10 cc of a 2.5 per cent solution should be administered. It is better to give an underdose than it is to administer an overdose, as otherwise the respirations may become too shallow during the induction of anesthesia by inhalation. After the patient shows signs of drowsiness and perhaps even stops counting, the gas mask is applied to the patient's face and nitrous oxide and oxygen is administered simultaneously with an injection of 1 cc of a 2.5 per cent solution of pentothal sodium about every 15 seconds. The respirations are watched all the time to see that breathing does not stop or is not markedly depressed. The results of this method are rather spectacular. The patient shows little or no signs of excitement, the blood pressure is decreased during the period of induction, as compared to the usual marked increase. The intratracheal tube may be introduced in about five or ten minutes, whereas previously it has taken two or three times as long. The amount of anes-

thetic (drop ether) used is about two-thirds as much as is necessary when no pentothal sodium is used. Patients have usually not become nauseated and have not vomited afterward. Shock is usually not in evidence postoperatively, although where extensive sympathectomy has been performed, the blood pressure may be more definitely lowered than it is in other cases.

The use of analeptic drugs for relief of respiratory depression has been tried with apparent success. The present status of the effects of several commonly used stimulants is controversial. However, I feel that such drugs as coramine (a 25 per cent solution of pyridine betacarboxylic acid diethylamide), metrazol (pentamethylene tetrazol), ephedrine and epinephrine may serve to support a depressed patient if used in addition to other measures. The route for the administration of the stimulant is the intravenous one.

Regional Anesthesia—The effects of regional methods of anesthesia have been increased by the substitution of metycaine [benzoyl- γ -(2-methylpiperidino)-propanol hydrochloride] for procaine. There are certain reasons why this occurred, one is that metycaine is a surface anesthetic as well as one effective by injection. The other reason is that the substitution of a 1 per cent solution of metycaine for a 1 per cent solution of procaine is not actually a substitution of an equivalent concentration. A 1 per cent solution of metycaine is approximately equivalent to a 1.25 per cent solution of procaine, so that in the statement that metycaine is more effective than procaine it must be admitted that the concentration of metycaine is relatively stronger than the concentration of procaine. The fact that metycaine is a surface anesthetic as well as an injectable one makes it of great value to the anesthetist, for the one outstanding unsatisfactory characteristic of procaine is that it is not a good surface anesthetic. It has been hoped that an agent could be produced with which one could carry out any method of local anesthesia. Metycaine is the nearest approach to this of any agent that has been developed up to this time. It was felt that metycaine would be a particularly satisfactory drug as a spinal anesthetic, and I admit that it is a good agent and that the anesthesia can be made to last longer than with procaine, but for operations which are to last an hour or less I still prefer procaine as a spinal anesthetic agent.

In various blocks, however, such as sacral block, cervical block, brachial plexus block, block anesthesia of the digits and field block, especially of the scalp, metycaine in a 1 per cent solution is definitely more satisfactory than a 1 per cent solution of procaine. I also should like to point out that in sacral block one finds results to be very much more encouraging with metycaine than with procaine. I prefer sacral block over spinal anesthesia for operations on the anus, because of the elimination of lumbar puncture headache. My experience with headache of this type has been that while it does not occur apparently as frequently as it did some years ago, one occasionally sees a patient who complains bitterly of headache for as long as two years after the operation. I have never been convinced that headache which lasts as long as this is very debilitating because subsequent events show that the period of recovery usually begins when unhappy circumstances in the life of the patient

are altered. Patients also complain very bitterly of headache with the hope that they can avoid paying the doctor's fee. In transurethral operations I have advocated the use of sacral block instead of spinal anesthesia because when undue distention of the bladder takes place the patient complains and in the event of spinal anesthesia the patient usually is not aware of the overdistention of the bladder. On the other hand, the surgeon has been better satisfied with spinal anesthesia and has become accustomed to avoiding marked overdistention of the bladder, under those circumstances spinal anesthesia is satisfactory. Here again, however, the question of headache has to be considered. The most persistent instance of headache that I have encountered was subsequent to one of these operations and spinal anesthesia.

For operations on the digits and when field block is used, it will be found that the metycaine will give postoperative relief of pain for several hours in most cases, while procaine does not. Most persons who have an idiosyncrasy to procaine and have a so-called novocain dermatitis can use metycaine without untoward results.

For celiotomy, especially on the upper part of the abdomen, I know of no block that is better than abdominal block, combined with gas, or gas and ether as an inhalation anesthetic, and moderate preliminary medication. The block of the abdominal wall may be carried out with a 0.5 per cent solution of procaine or metycaine, which should contain a small quantity of epinephrine (6 minims of 1:1,000 solution in 200 cc. of the anesthetic solution). The block should be done 15 to 20 minutes before the incision is to be made so that there is an opportunity for the solution to soak into the tissues and permeate entirely the terminations of the intercostal nerves. Under such circumstances it is presumed that the injection of the solution into the abdominal wall will be made when the general anesthesia has been induced. The general anesthesia may be lightened or discontinued as soon as the peritoneum has been closed.

To combine local and general anesthesia is often desirable, but when spinal anesthesia is combined with general anesthesia it is best in my experience to give the spinal anesthetic at least 10 to 15 minutes before administration of the general anesthetic is started. If in the course of the operation spinal anesthesia becomes sufficiently high so that the patient becomes dyspneic, one will find that respiration becomes very annoying as the patient makes the vigorous effort necessary to ventilate himself. There is danger that the induction of general anesthesia, taking place simultaneously with the production of spinal anesthesia, will bring the patient into a dangerous degree of narcosis when the spinal anesthesia has produced its maximal effect and the general anesthesia has produced its maximal effect. I have seen one fatality because of such an occurrence.

For the support of the blood pressure during spinal anesthesia, I prefer to inject intramuscularly 25 mg. of ephedrine just before spinal anesthesia is induced, and to administer 25 mg. of ephedrine intravenously during anesthesia if the systolic blood pressure falls below about 85 Mm. of mercury.

Individual variations in the patient's reaction to the anesthetic and the stimulant may be more nearly balanced than by routinely using a larger initial dose of the stimulant

The present need for a better noninflammable anesthetic has made the combined use of regional and intravenous anesthesia advantageous. Fortunately, most of the barbiturates have an antispasmodic action while most local anesthetics produce a spastic effect when the patient exhibits a toxic reaction. This antagonistic effect of a local anesthetic compared with an intravenous barbiturate makes their combined use one that tends to increase the safety of the use of each agent. In some instances the use of an intravenous anesthetic at first, followed by the blocking of the nerve trunks while the patient is unconscious, is greatly appreciated by patients.

Preliminary medication is advisable before regional methods of anesthesia are to be used. For the average adult, I like to give pentobarbital or nembutal, $1\frac{1}{2}$ gr (0.1 Gm), the night before operation and repeat this dose about 7 A M on the day of operation, and to administer $\frac{1}{6}$ gr (0.01 Gm), of morphine and $\frac{1}{150}$ gr (0.0004 Gm) of atropine by hypodermic injection, 40 minutes before the operation. This procedure is usually satisfactory. However, during the operation, if the patient seems to be suffering regardless of whether or not the anesthesia is beginning to wear off, of whether or not the operation is more extensive than planned for, or of whether or not the anesthesia is insufficient for the contemplated operation, a small dose of morphine will usually relieve the patient of his pain. In some cases the ordinary dose of morphine is insufficient and an additional amount of morphine is necessary to give relief. This should be given intravenously. The intravenous injection should be carried out very slowly and should be discontinued as soon as the patient feels some effect of the drug. If more is to be administered, a period of ten minutes should elapse before any further morphine is given intravenously. The usual dose for intravenous administration is less than the dose that is given subcutaneously. That is, if one would give $\frac{1}{4}$ gr (0.016 Gm) subcutaneously, one would administer $\frac{1}{6}$ gr (0.01 Gm) intravenously. One-eighth grain (0.008 Gm) of morphine intravenously is equivalent to $\frac{1}{6}$ gr (0.01 Gm) given subcutaneously.

REFERENCE

- ¹ Waters, R. M., Hathaway, H. R., and Cassels, W. H. The Relation of Anesthesiology to Medical Education. J A M A, 112, 1667-1671, April 29, 1939

SYMPATHETIC NERVE BLOCK AS AN ADJUNCT ANESTHESIA IN MINIMAL RESECTION OF THE STOMACH FOR PEPTIC ULCER *

WILLIAM FRANCIS RIENHOFF, JR., M.D.
BALTIMORE, MD

FROM THE DEPARTMENT OF SURGERY OF THE JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD

THE OBJECT of this report is twofold. In the first place, to present a series of consecutive cases of benign ulcers of the pyloric antrum and the duodenum which have been treated by partial gastrectomy, performed under a very light nitrous oxide and oxygen inhalation analgesia, combined with an intra-abdominal injection of a weak solution of pontocaine into the celiac plexus, and in the second place, to describe an operative technic, based upon anatomic and physiologic considerations, that combines safety and efficacy, as far as the immediate and late postoperative results are concerned, in a higher degree than the more conservative and also the more radical procedures.

Material—The basis of this report consists of a series of 82 consecutive cases of pyloric and duodenal ulcer that have been operated upon by various operators employing the same surgical technic, but different methods of anesthesia. The operation in each instance has been a resection of only the pyloric antrum followed by a short loop antecolic gastrojejunostomy. Forty-four patients have been operated upon by different operators, under general anesthesia, *ie*, nitrous oxide and oxygen induction, followed by ether with a preceding basal anesthesia such as avertin. Five deaths occurred in this series, a mortality rate of 11.3 per cent, only one of which could be attributed to the operative procedure. In the latter case, the patient was found at autopsy to have developed an acute pancreatitis that might have been caused by the operative dissection of a large penetrating and indurated ulcer away from the head of the pancreas. Three deaths followed the development of bronchopneumonia and one, four hours after operation, during a generalized convulsion. The latter patient had been given a combined general anesthesia, *ie*, avertin and cyclopropane. Postmortem examination in all of these patients revealed *per primam* healing of the gastrojejunal anastomosis as well as the duodenal stump, so that in at least four, if not all five, the lowering of the patient's resistance and vitality due to the general anesthesia played a major rôle in causing their death.

In striking contrast to this is a series of 38 consecutive patients that were operated upon in whom, although the same surgical technic was employed as in the above series, sympathetic nerve block and analgesia was used in preference to general anesthesia (Table I). In this series no deaths occurred.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

ANESTHESIA IN STOMACH SURGERY

TABLE I

IDENTIFYING DATA RELEVANT TO THE 38 PATIENTS WHO
RECEIVED SYMPATHETIC NERVE BLOCK

R R, Hosp No 148480	F R, Hosp No 148057
J M, Hosp No 150340	E S, Hosp No 106285
J M, Hosp No 152636	B G, Hosp No 143206
G U, Hosp No 150914	B D, Hosp No 143090
F B, Hosp No 152775	H M, Hosp No 111689
A B, Hosp No 152908	C S, Hosp No 110025
M C, Hosp No 155005	N H, Hosp No 72117
J P, Hosp No 160111	J J, Hosp No 72599
M P, Hosp No 160146	L Z, Hosp No 74631
R W, Hosp No 160504	J R, Hosp No 127170
J S, Hosp No 163287	C M, Hosp No 127529
H B, Hosp No 100764	D W, Hosp No 130947
C W, Hosp No 143641	L S, Hosp No 130930
W Q, Hosp No 103075	B C, Hosp No 170793
F F, Hosp No 103106	J G, Hosp No 170430
C A, Hosp No 103163	R S, Hosp No 170387
J W, Hosp No 106035	C H, Hosp No 167878
W G, Hosp No 71840	C M, Hosp No 168231
W M, Hosp No 127682	L M, Hosp No 164296

In four of this latter group, the patients had developed marginal ulcers following a posterior gastro-enterostomy previously performed elsewhere for duodenal ulcer. In two of these four, the marginal ulcers had penetrated the colon resulting in gastrojejunal fistulae. In the latter two cases, a resection of part of the jejunum and transverse colon was found to be necessary as well as a resection of the pyloric antrum and first portion of the duodenum. An end-to-end anastomosis was performed in both cases on the jejunum and colon. In the former two cases of marginal ulcer, the jejunum was simply closed and the stomach resection carried out as herein described. Even in these complicated cases there were no untoward respiratory or abdominal sequelae following the use of celiac sympathetic nerve block anesthesia.

Further advantages of combined local anesthesia and gas analgesia over general anesthesia will be alluded to under Discussion.

Anesthesia—The present literature on the employment of a local, in combination with a very light gas anesthesia for abdominal operations is extensive. Crile,¹ in 1915, was the first to point out the advantages of anoci-association and the prevention of shock as well as many other postoperative complications by the use of a combination of local and very light gas anesthesia. Finsterer² has employed local and splanchnic nerve block anesthesia for years. For a complete bibliography of the development of the methods of local anesthesia in abdominal surgery, one should consult the monograph entitled *Anesthesia in Abdominal Surgery*, by Hans Finsterer, published in 1923.

The only modification of the previous methods to be noted in this report is the employment of a "light" gas analgesia while going through the abdominal wall and opening the peritoneal cavity. The patient is then allowed to rebreathe into the gas bag throughout the operation without further addition of

nitrous oxide The celiac plexus is injected intra-abdominally at the level of the twelfth thoracic vertebra (Fig 1) with 100 cc of a 1:3,000 solution of pontocaine which is allowed to diffuse in the retroperitoneal tissue In this manner a concentrically radiating area of retroperitoneal edema may be observed which extends over the visible area of the posterior peritoneal wall and

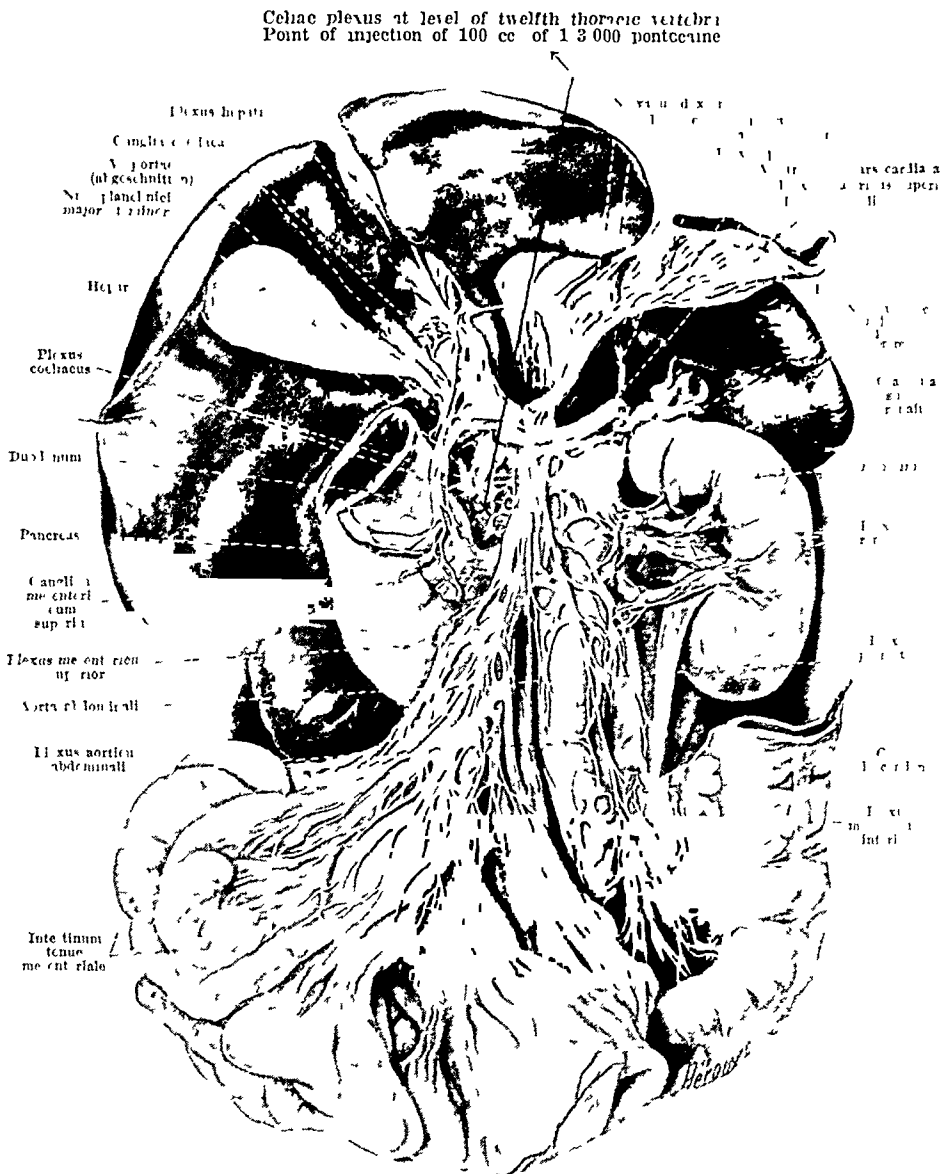


FIG 1—Abdominal plexuses of the sympathetic (Stålholz, Hand Atlas of Human Anatomy, vol 3)

bathes the entire celiac sympathetic plexus with the pontocaine solution The technic of injection is greatly facilitated by the use of a long, guarded needle devised by Finsterer The left hand is inserted into the supraduodenal fossa to the left of the gastrohepatic omentum Just below the inferior surface of the liver, or portal hilus, the right border of the aorta is located with the index finger The middle finger alongside the index finger will thus impinge upon the surface of the tissue lying between the aorta and the inferior vena cava

The guarded needle is then inserted into the retroperitoneal tissues, being held in the right hand and guided by the groove between the middle and index finger of the left hand. The sharp point of the needle may be felt to engage the bony structure of the body of the twelfth thoracic vertebra. A 20 cc syringe is attached and the needle very slightly withdrawn. A few cubic centimeters of the pontocaine solution are then injected, but the plunger is again withdrawn to be certain the needle point is not inside a blood vessel. If no blood is recovered in the syringe, the 100 cc of the pontocaine solution are injected slowly over a period of about three minutes. Within a very short time the increased relaxation of the abdominal wall can be appreciated. Although the patient is receiving just enough nitrous oxide and oxygen to quiet him psychically, the degree of relaxation of the abdominal wall throughout the operation remains constant. There is no straining or tendency to become alternately light or deep as is so often the case with gas anesthesia when used alone without some supplement.

Operative Procedure—The rationale for the operation employed in this series of cases is based upon anatomic and physiologic data, which seem to indicate that the lower fifth of the stomach or the pyloric antrum may truly be considered the "pacemaker" of this organ.

In 1906, Edkins³ showed that a decoction made by boiling pyloric mucous membrane with acid or with water or with peptone and injected in small quantities into the jugular vein caused a secretion of gastric juice, containing both hydrochloric acid and pepsin. In order to produce this positive effect, it was necessary to employ pyloric mucous membrane from the lower fifth of the stomach. Extracts made from the mucous membrane of the remaining portions of the stomach proved to be ineffective. The secondary secretion of gastric juice is determined, not as Pavlov and Popielski⁴ imagined, by a local stimulation of the reflex nervous apparatus in the gastric wall, but by a chemical mechanism. The first products of digestion act on the pyloric mucous membrane and produce in this membrane a substance which is absorbed into the blood stream, and carried to all the glands of the stomach, where it acts as a specific excitant of their secretory activity. This substance has been named gastrin and is a gastric hormone. This form of chemical stimulation for the formation of gastric juice persists long after the mental effects or memory of a meal has worn off, as well as the psychic secretion through the vagi, described by Pavlov.

As a result of numerous physiologic experiments since, the original observations of Edkins³ have been corroborated.

The presence of gastrin in human postmortem pyloric mucous membrane has been demonstrated by Ivy, *et al*,⁵ and shown to be present to the same extent as in hogs' mucosa. The similarity of gastrin to histamine has been demonstrated by Koch, Luckhardt, *et al*,⁶ who think it is a basic imidazole derivative. Thus far pilocarpine and histamine are the only known imidazole derivatives which stimulate the gastric mechanism to secretion. Further McHenry and Best⁷ (1930), having developed histaminase, a histamine in-

activating enzyme, enabled Sacks, Ivy, *et al*⁸ (1932), to demonstrate that this enzyme will inactivate the active secretory agent in extracts of the pyloric mucous membrane. This again demonstrates the close relationship of this active principle, gastrin, to the imidazole ring. If one concedes that histamine and gastrin are identical, then the former produced in physiologic amounts by the pyloric mucous membrane may be viewed as not only being a specific hormone, augmenting and facilitating the formation of gastric juice, but also, as shown by Koskowski and Ivy⁹ (1925), increasing the motor activity of the gastro-intestinal tract as well. This view is supported by Best and McHenry⁷ (1930), on the distribution of histamine and histaminase in the tissues of the body. They found that the stomach and liver are the only organs examined in the body which contain relatively large quantities of histamine and which do not also contain histaminase. The enzyme is absent from the stomach and practically absent from the liver. From their work we can say that it is easily possible for the pyloric mucosa to liberate enough histamine into the portal blood and then into the general circulation to stimulate the production of acid by the gastric glands and to exercise synergistic action on the digestive process.

Removal of the pyloric antrum must, therefore, take away one, if not the major, factor in the stimulation of the formation of gastric juice, *ie*, acid and pepsin, as well as have a retarding influence upon gastric motility.

Although peristaltic waves begin in the cardiac end of the stomach, the incisurae produced by their contractions are very much deeper when they reach the lower fifth of the stomach. The pyloric antrum, on erect fluoroscopic examination in the majority of individuals, appears to be merely a continuation upward of the intestinal tube, when compared to the sac-like, relatively atonic, fundic portion of the stomach. Whether peristaltic waves of contraction may arise independently near the beginning of the pyloric antrum in the distal four-fifths of the stomach has not yet been proved, but it is an objective certainty observed fluoroscopically that the lower fifth of the stomach is far more active from the standpoint of the number of contraction waves, as well as the extent of their contractions. The difference in the thickness of the muscle layers of this region of the stomach, together with its well known triturating effect on food, would lead to the expectation of the observed increased contractility of this region. It would seem likely, in our present state of knowledge, that pain associated with ulcerative lesions of the stomach has its origin, in part at least, in the muscular spasm of the pyloric sphincter and antrum associated with the usual hyperperistalsis, hypertonicity and hyperacidity. Thus the relief of pain may in a large measure be directly attacked by the removal of this region of the stomach which manifests the rôle of an accelerator or amplifier of previously initiated muscular activity. In this manner three important steps have been taken in ridding the patient of an ulcer, and also in protecting him from the liability of a recurrence. These steps are (1) The removal of the portion of the stomach which is most active, from the standpoint of motility and contractility, and therefore that portion the mucous membrane of which is subjected to the

highest incidence of trauma, (2) the ablation of the area of mucous membrane which is productive of a hormone similar to histamine, and responsible for, in contrast to the psychic secretion, the chemical secretion of gastric juice, (3) the shunting of gastric contents away from the remaining potential ulcer bearing area in the duodenum

Operative Technique—A midline incision has been employed (Plate I) because exposure of the lesser curvature of the stomach, and thus the left gastric artery and coronary vein, is more easily accomplished with less vigorous

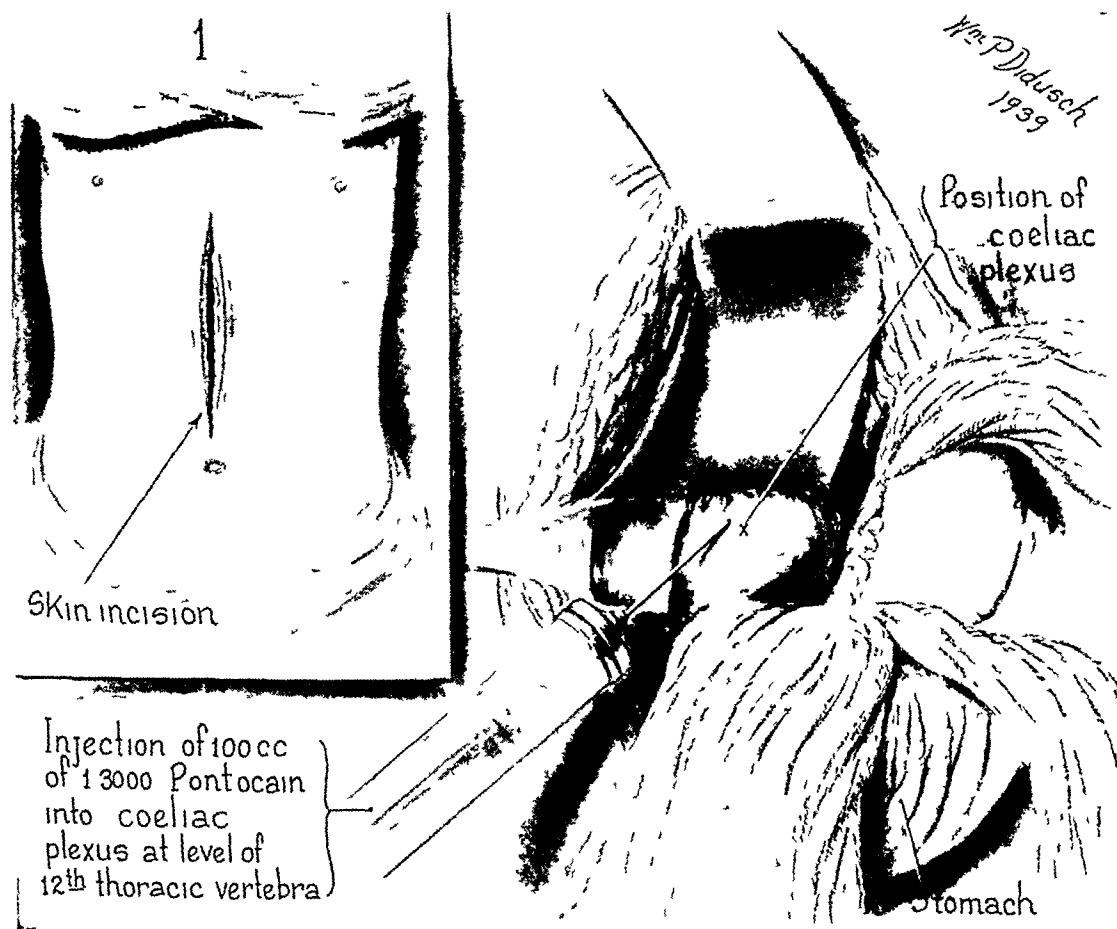


PLATE I—FIG 1 Midline incision extending from linea alba

FIG 2 shows posterior peritoneal wall with needle projecting into retroperitoneal tissue, at the level of the coeliac plexus

retraction by this route than through a high right rectus incision. The less the degree of retraction the better the relaxation of the abdominal wall. In the upper abdomen the midline incision traverses the linea alba which is the most avascular portion of the abdominal wall. Obviously, there is no interference with the nerve supply to the rectus muscle or further weakening of that structure from direct trauma in splitting its fibers. The round or falciform ligament of the liver lies immediately beneath the linea alba, but under the right lip of the incision, the reflection of the peritoneum to cover the ligament may be incised and the entire body, *i e*, ligament, fat and peritoneum, reflected laterally. When the peritoneum is incised somewhat to the right of the reflection of the round ligament, it is not necessary to suture the edges of

the former when closure of the abdomen is made. The round ligament falls into its normal position, covering the posterior surface of the wound as a peritoneal flap, when the linea alba and thus the abdominal wall is closed.

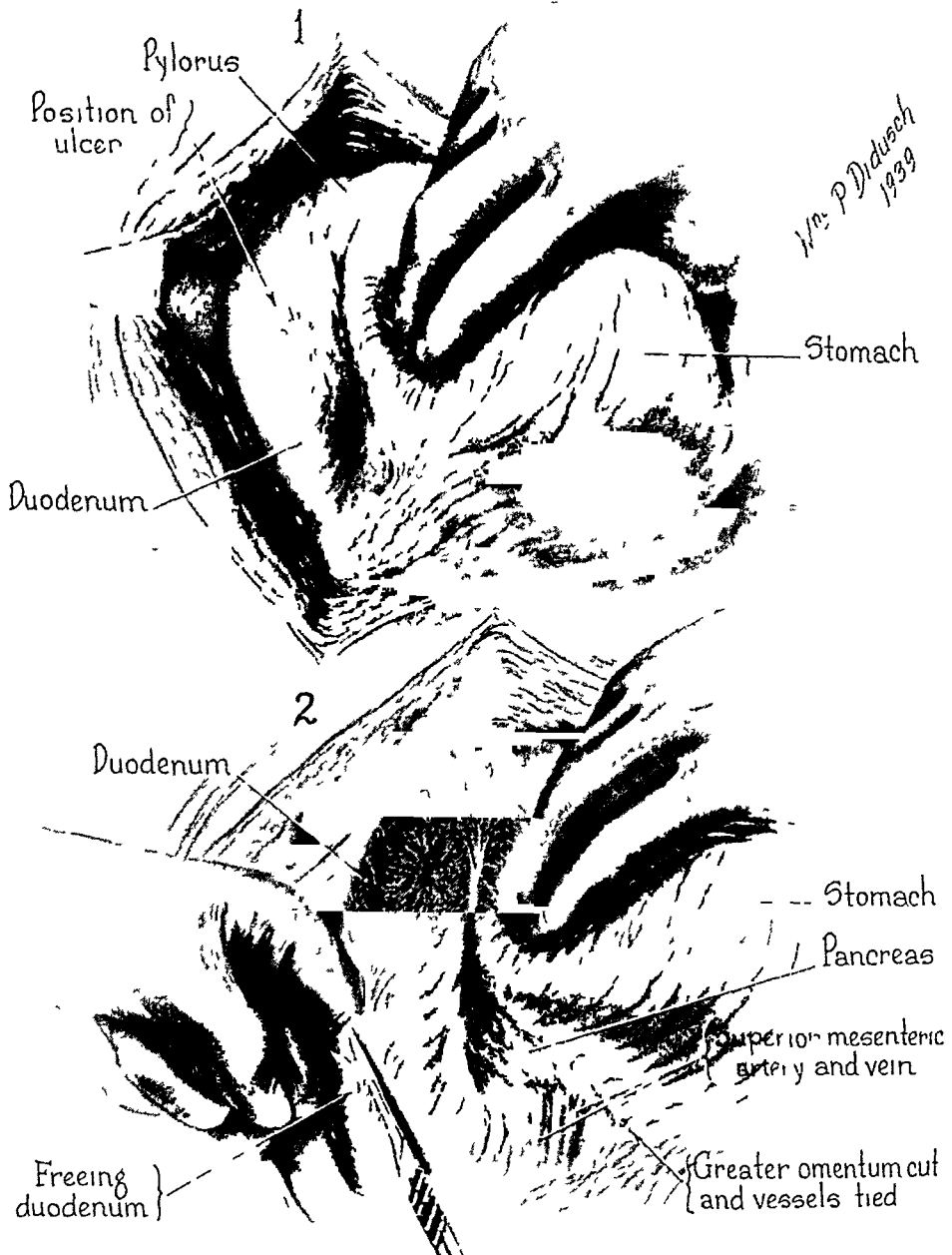


PLATE II—FIG 1 Stomach delivered through incision, showing position of ulcer in the posterior part of the second portion of the duodenum

FIG 2 Mobilization of the second portion of the duodenum, by incising the lateral peritoneum

Following a thorough examination of the abdominal contents, the injection of the retroperitoneal tissues in the region of the celiac plexus is accomplished as described above (Plate I, Fig 2)

The location of the common duct and its point of disappearance behind the upper part of the second portion of the duodenum has been made a

routine preliminary step in the operation. The knowledge of the position of this duct affords not only more confidence but also more safety in a liberal mobilization of the second part of the duodenum for resection of ulcers in this region. At the same time, such a free dissection enables the operator to effect a more secure closure of the duodenal stump (Plates II and III). The left gastric vessels and right vagus nerve are then divided and ligated with medium "c" silk. Following this, vessels running in the gastrohepatic and gastrocolic as well as the duodenohepatic and duodenocolic ligaments are individually clamped and ligated with "c" silk. Thus the entire lower fifth or pyloric antrum of the stomach, together with the first and upper two-

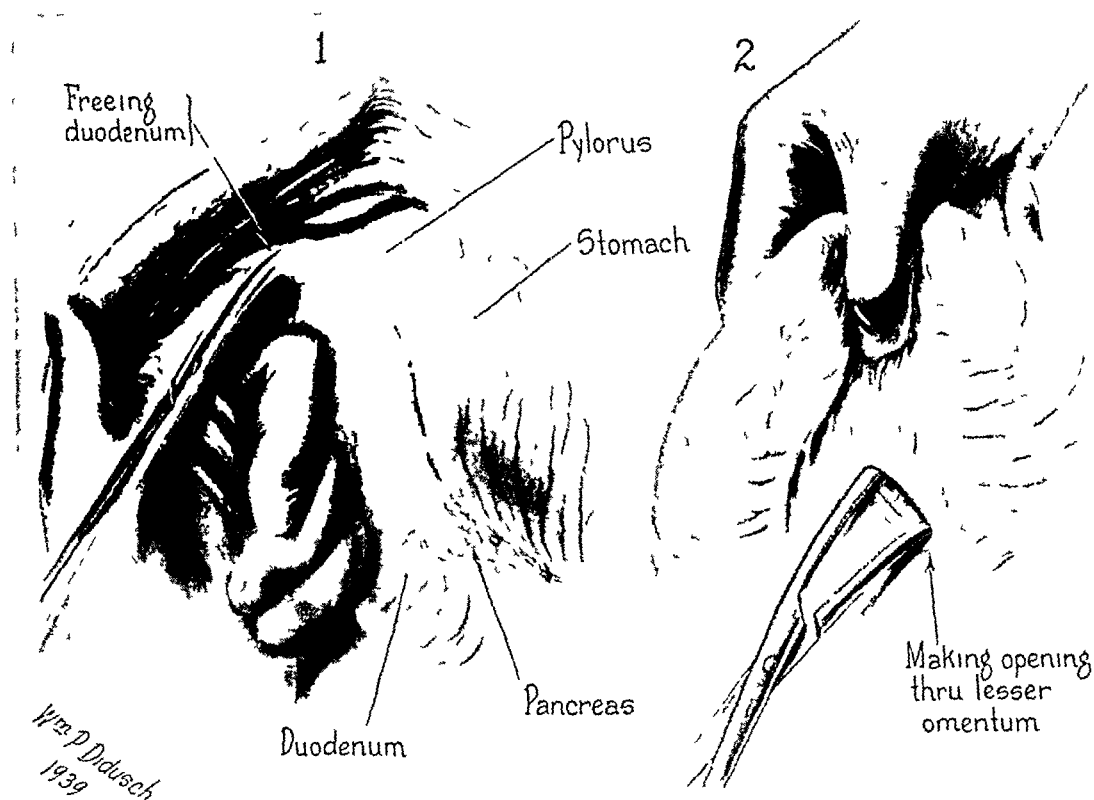


PLATE III—FIG 1 Further mobilization of the first part of the duodenum by separating the gastrohepatic omentum

FIG 2 Curved clamp inserted into opening of gastrocolic omentum, making an opening in the lesser peritoneal curvature

thirds of the second portion of the duodenum, are thoroughly mobilized and the latter freed from the head of the pancreas. A medium sized Payr crushing clamp is now placed across the body of the stomach at approximately the junction of the fundus and the pyloric antrum (Plate IV). The stomach is divided and the posteromedial surface of the duodenum is freed from the head of the pancreas. Due to the fact that the common duct lies between the head of the pancreas and the medial wall of the duodenum, a large portion of the latter may be removed without danger of injury to the former. The duodenum, having been mobilized below the ulcerated area, is clamped across with a small Payr crushing clamp (Plate V). The pyloric antrum, pyloric sphincter, first and part of the second portion of the duodenum are then removed together with the ulcer. The stump of the duodenum is closed

with two layers of suture (Plate VI), the first a continuous suture of "o" chromic catgut. This is placed underneath the crushing clamp in such a manner that the crushed tissue beyond it can be cut off without danger of

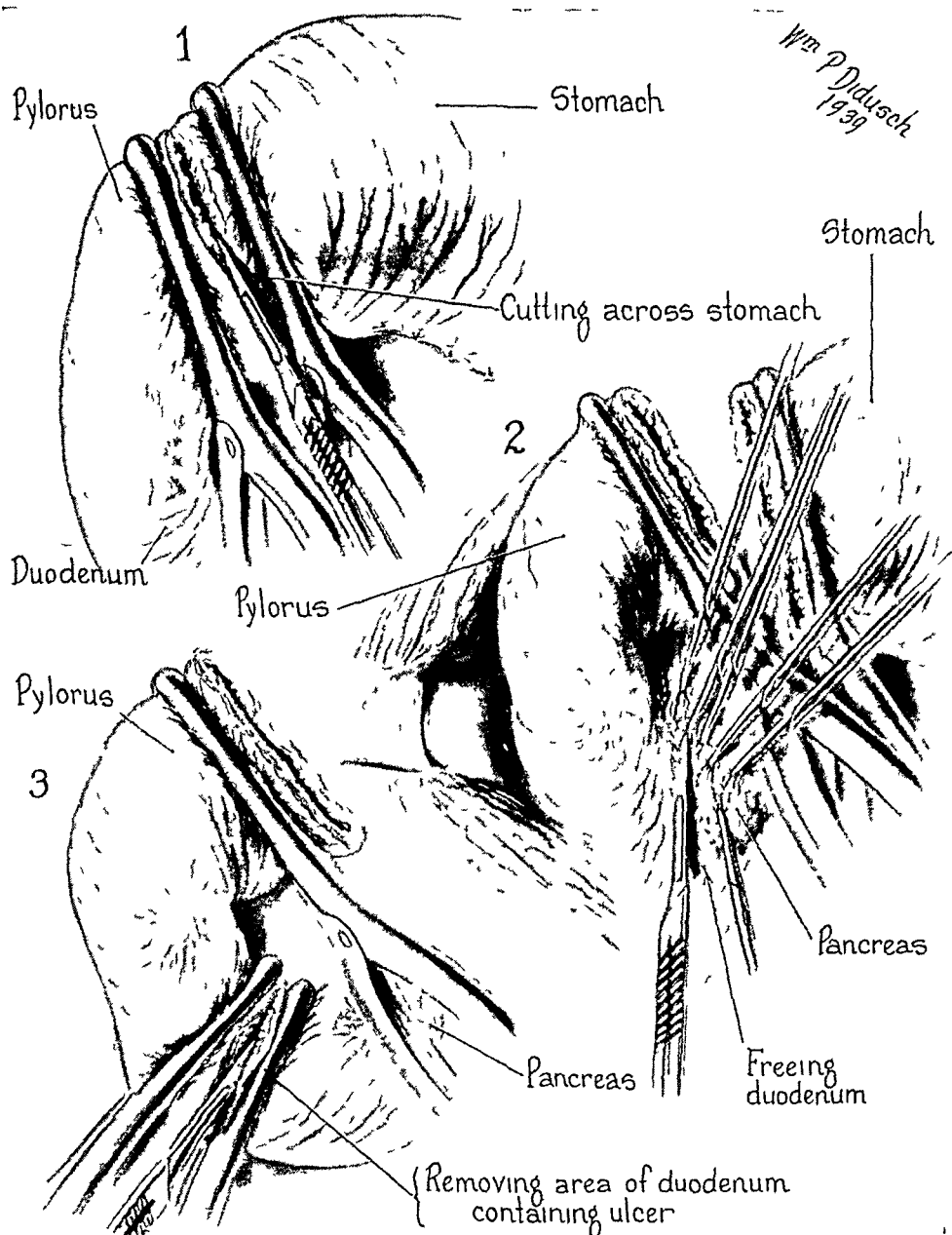


PLATE IV —FIG 1 Division of stomach just proximal to pylorus. This illustration is somewhat misleading as more stomach is removed than demonstrated in this illustration. The impression from this would lead one to believe that less than the lower fifth of the stomach is excised. The proximal Payr clamp is also larger than the distal one on the duodenal side.

FIG 2 Dissection of the pyloric end of the stomach and first portion of the duodenum from the head of the pancreas.

FIG 3 Division across the duodenum in the second portion, removing that portion containing the ulcer.

cutting the suture line. The advantage of removing this crushed tissue, which will become necrotic, is obvious. With this type of suture only viable tissue is turned in. Interrupted Halsted sutures of fine "a" silk are then used to

invert the first continuous suture line. All bleeding points about the head of the pancreas are transfixed with fine silk. This procedure is felt to be important because the pancreatic tissue cut across in the freeing of the second portion of the duodenum may, if not sewn up, give rise to a drainage of

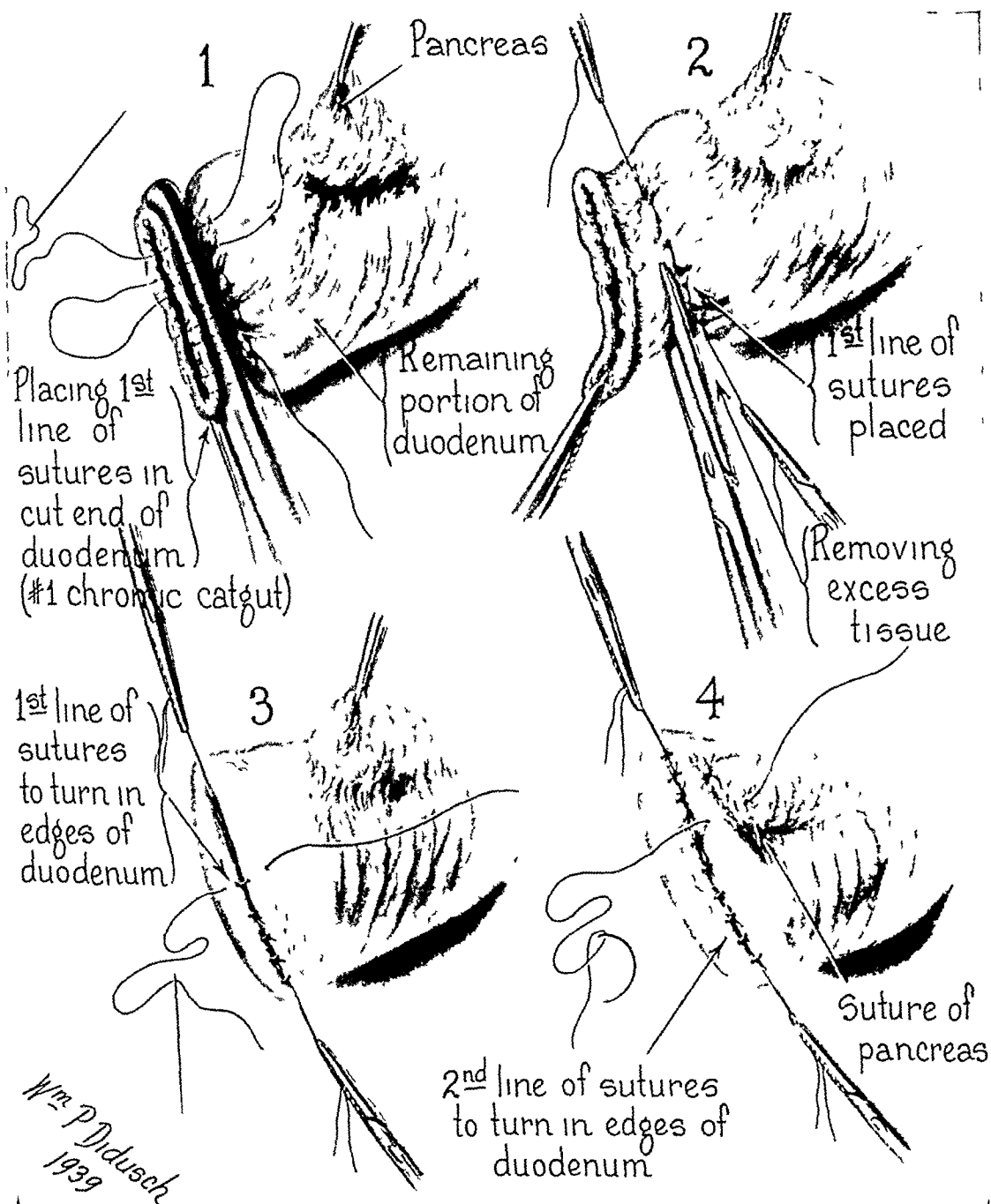


PLATE V—FIG. 1. Demonstrates the method of closure of the duodenum. A continuous mattress suture distal to the Payr clamp is placed so the crushed tissue can be excised as shown in Figure 2, leaving only viable tissue to be turned in with interrupted silk sutures as shown in Figures 3 and 4.

pancreatic ferments that will precipitate a peritonitis similar to that seen in acute pancreatitis. Care is taken to insert a small part of the beginning or extreme right portion of the gastrocolic omentum between the raw surface of the head of the pancreas and the duodenum, in order to prevent any possibility of digestion or erosion of the stump of the latter. Attention is

then turned to the reestablishment of the continuity of the gastro-intestinal tract. Due to the relatively small segment of stomach removed, a short-

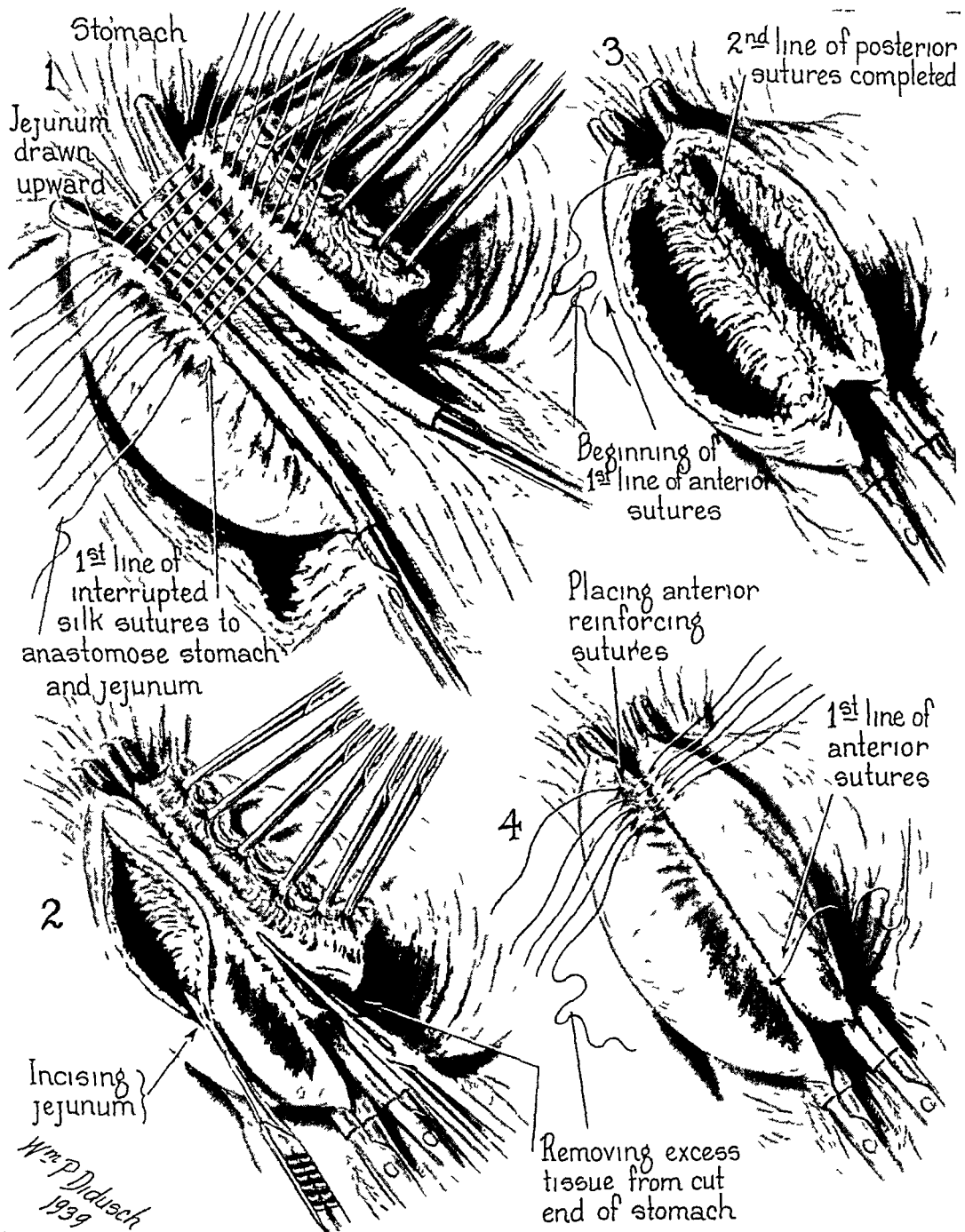


PLATE VI—FIG 1 demonstrates Halsted's interrupted sutures placed in position before tying making up the posterior row. Also the noncrushing intestinal clamps in place, both on the stomach and jejunum. A gauze net webbing is used as a sleeve over the clamp blades rather than rubber. FIG 2 demonstrates opening the jejunum, also trimming away of the crushed, devitalized tissue, resulting from the use of the Payr clamp. FIGS 3 and 4 show the inner and outer layer of sutures. The inner layer is continuous No. 1 chromic catgut.

looped antecolic gastrojejunostomy can be performed readily and without the necessity of an entero-enterostomy. The colon and greater omentum are

returned to the peritoneal cavity by shunting them to the left of the proximal loop of the jejunum. When this latter portion of the intestine is sewn to the cut end of the stomach, the distance between Treitz's ligament and the beginning of the gastrojejunal anastomosis at the lesser curvature of the stomach is

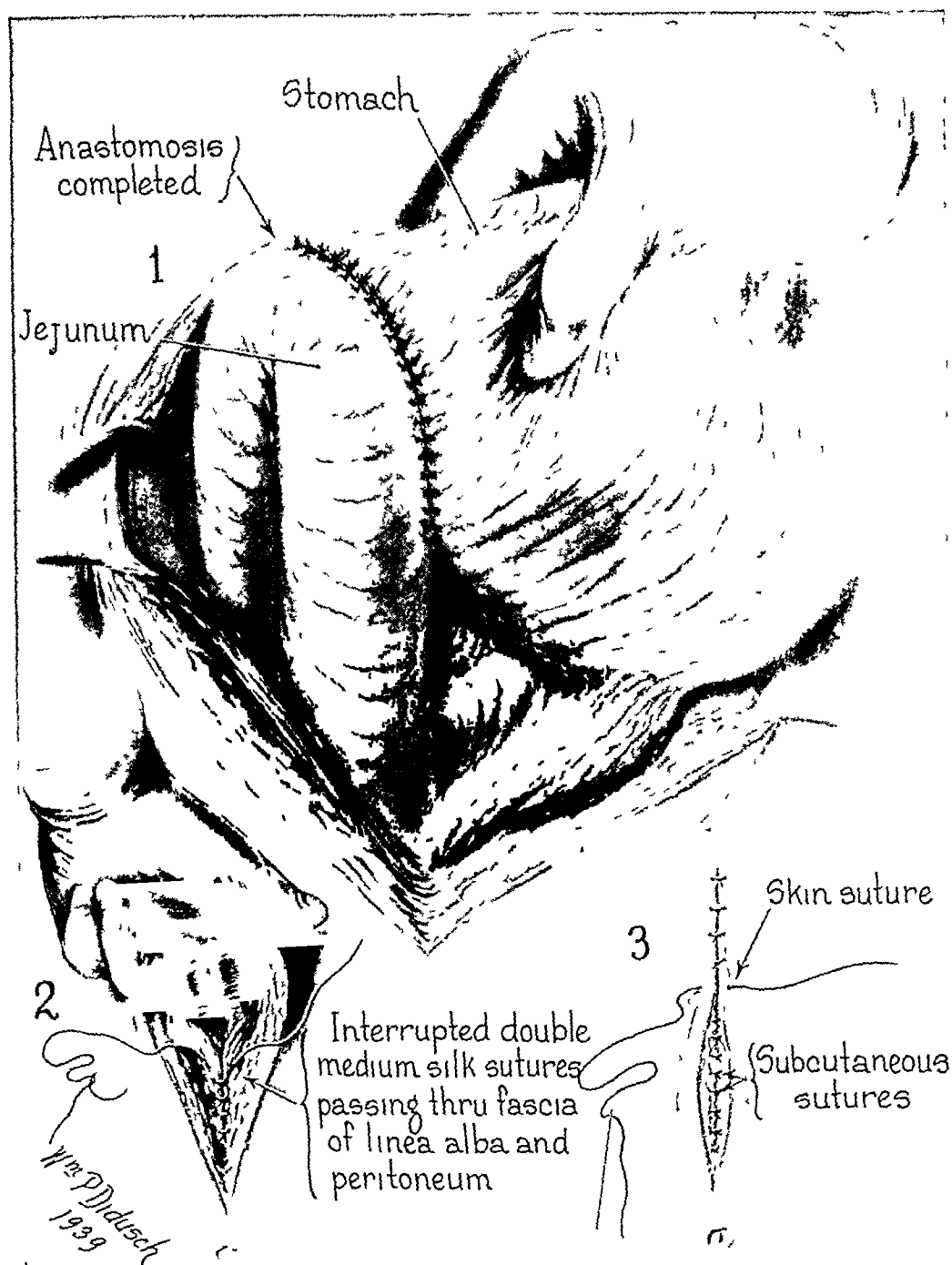


PLATE VII—Demonstrating the anastomosis completed, the proximal end of the jejunum to the lesser curvature of the stomach in Figure 1, closure of the abdominal wall with interrupted medium silk in Figure 2, and the skin in Figure 3. No stay sutures used.

only three fingers' breadth. A few centimeters proximal to the Payr crushing clamp, a noncrushing clamp is placed upon the stomach and a similar one upon the jejunum. Gauze webbing is used to cover the blades of the noncrushing intestinal clamps in preference to rubber, the former having the advantage of

being far less bulky and affording much greater purchase, and therefore, capacity to hold with less pressure exerted on the tissue through the blades of the clamp. The Payr crushing clamp is then removed and mucosa clips are placed upon the cut end of the stomach embracing only the crushed portion of the stomach wall, while the imprint of the Payr clamp is plainly visible (Plate VI). Halsted interrupted fine silk sutures are then inserted about 0.5 cm apart, as the posterior suture line. The entire suture line is placed before any of the sutures are tied, thus allowing more room for inserting successive sutures accurately than if they are tied as placed. The crushed portion of the stomach wall, which has been grasped by the mucosa clips, is then excised. The posterior interrupted suture line is much more easily and accurately placed if the mucosa clips are allowed to remain on through this step in the operation. This is due to the fact that the clips, lying in such a manner that their handles point to the left, cause the posterior wall of the stomach to be thrown anteriorly and place it in a more convenient position for suturing. The jejunum is then opened and a continuous suture of No. 1 chromic catgut is placed as an internal suture line in both the posterior and anterior lips of the mucosa. These stitches are locked only at the ends, to prevent any chance of diminution of the stoma by constriction. The final anterior row of Halsted interrupted "a" silk sutures is placed in position before the noncrushing intestinal clamps are removed, but they are not tied. This is accomplished after the stomach and intestine have been released from the noncrushing clamps. In this manner the sutures are more accurately placed and then tied without exerting any tension on the wall of the viscera. A couple of interrupted sutures are placed between the lateral wall of the proximal loop of the jejunum and the transverse mesocolon to prevent a loop of jejunum lower down from slipping through this potential opening. The anastomoses have so far been made isoperistaltic with the proximal loop sewn to the lesser curvature.

The abdomen is closed in the following manner. The linea alba with interrupted double medium silk and the skin with interrupted fine silk sutures (Plate VII).

Discussion—The use of combined anesthesia is not new, but the employment of a very light nitrous oxide and oxygen analgesia together with the creation of a block of the abdominal sympathetic nervous system, in operations upon the stomach, forms a different combination than heretofore used. The inevitable fall in blood pressure that occurs when only local and splanchnic anesthesia is employed is avoided by the stimulating effect of the nitrous oxide and oxygen. Entirely aside from the anesthetic effects of local infiltration, in and about the celiac sympathetic plexus, is the resultant block in this nervous pathway both to and from the stomach and small intestine. It would seem that the interruption of efferent impulses from the operative field to the higher centers may play an important rôle in the prevention of operative as well as postoperative shock. Regardless of the length of time occupied by the operative procedure, there has been no instance of shock during or after the opera-

tion in any one of this series of 38 patients. In fact, no elevation of the pulse rate or fall in blood pressure has occurred either during or after the operation. Relaxation of the abdomen during the operation is fully as complete, if not more so, than with a general anesthetic. However, even more striking is the uncomplicated smoothness of the immediate postoperative period of convalescence, the first four or five days, of those patients in whom the sympathetic block anesthesia has been made, compared to those who have been given a general anesthesia. The patients in which sympathetic nerve block has been used were almost entirely free from nausea, vomiting, distention and meteorism encountered in the comparative series of cases similarly operated upon, but in which general anesthesia of one type or another was employed. In the latter group the hospitalization was uniformly longer and in many instances this was undoubtedly due to the debilitating effect of a not fatal but severe pulmonary infection or metabolic disturbance pursuant to the inability of the patient to resume his normal fluid intake immediately after operation. It is believed that the sympathetic nerves to the stomach and small intestine provide mainly the inhibiting fibers that give rise to positive dilatation or relaxation preceding a contraction wave, the impulse for which comes largely through the vagi. In a few cases of intractable bronchial asthma in which the thoracic trunk of the vagus nerve was interfered with, there resulted a most severe or obstinate distention of the highest degree. It is likewise felt that the temporary removal of or interference with the function of the sympathetic nerve impulses thus has a tendency to prevent distention, meteorism and stasis by procuring in this manner an unantagonized vagotomic effect. Resection of the pyloric antrum for peptic ulcer of this structure or the duodenum is felt to be desirable because

(1) From fluoroscopic observations the pyloric antrum or "pyloric mill" is the most active portion of the stomach from the standpoint of tonic and peristaltic contraction. That such muscular activity in the gastro-intestinal tract is productive of symptoms even in the absence of ulcer is a well known clinical fact.

(2) Recent physiologic observations have established, beyond peradventure, that the chemically stimulated gastric secretion, in contradistinction to the psychic secretion, is more prolonged than the latter and results from the secretory activating influence of a hormone, "gastrin." The latter is produced almost entirely in the mucous membrane of the pyloric antrum. The total ablation of this portion of the stomach removes from the secretory chain one of the major links in the secretory mechanism. The proof of this assertion is to be found in the follow-up examination of these patients. Over 85 per cent of them have been examined. In each of these, a plain, in some, an alcohol, test meal has been employed. In two patients only has there been a persistence of a high free and combined acid, but both of these are symptom free and perfectly well. In the remainder examined there has been either no free hydrochloric acid or a very small amount with a low combined acidity. The time elapsing since operation varies from four years to six months, and, so far,

there have been no instances of definitely detectable recurrence of an ulcer or marginal ulcer at the site of the gastro-jejunal anastomosis. Hemorrhage recurred three times in each of two patients following operation. One is at present in the Johns Hopkins Hospital recovering from a severe hemorrhage, the source of which is unknown at present. The other, a medical student, is now well and at work. The source of his postoperative hemorrhage was likewise undetermined. Fluoroscopic examination of these postoperative stomachs has shown the emptying time to be slightly faster than normal.

(3) The remaining portion of the second part of the duodenum is placed at rest by shunting food and gastric secretion away from this potentially ulcer bearing area.

From the technical side, the short-loop, antecolic gastrojejunostomy has these points to recommend it:

(1) It is probably the simplest of gastric resections to perform, and is apparently efficacious.

(2) The mortality is much less than in the more extensive resection and the ultimate postoperative results are equally as good.

(3) If further operative procedures should prove necessary, more stomach remains to operate upon.

(4) The antecolic is to be preferred to the retrocolic anastomosis because the proximal loop of jejunum is just as short in the former as in the latter. Further, the complications that not infrequently are precipitated by the mesocolon are thus avoided.

(5) With such a short proximal loop in the jejunum, an entero-enterostomy is unnecessary. The length of jejunum from Treitz's ligament to the beginning of the anastomosis is not over three fingers' breadth.

(6) The removal of devitalized tissue by the crushing clamp enhances primary healing of the suture lines.

(7) Attention is called to the continuous suture distal to the small Payr crushing clamp on the duodenum. This suture line is placed in viable tissue beyond the clamp so that when the crushing clamp is removed and the crushed tissue trimmed away, the subsequent inverting Halsted interrupted sutures turn in only healthy tissue. In other methods of sutures, such as the Parker-Kerr, there remains a line of clamped necrotic tissue in an infected blind pouch. It would seem better to remove this tissue.

CONCLUSIONS

(1) A combination anesthesia consisting of sympathetic nerve block with a light nitrous oxide and oxygen analgesia has given excellent results in resection of the stomach.

(2) Resection of the pyloric antrum or "pacemaker" of the stomach combines the attributes of simplicity and safety as well as the restoration of the production of gastric secretion to approximately normal.

(3) Extensive resections of the stomach are far more hazardous and no more efficacious in the great majority of cases.

(4) Thus minimal resection of the stomach, removing only the pyloric antrum, is a rational procedure based on known anatomic and physiologic data, and from the standpoint of immediate and postoperative results is sufficiently radical to restore the patient to a normal state of health in the great majority of instances

REFERENCES

- ¹ Crile, G W Alcalescence, Acidity Anaesthesia, A Theory of Anaesthesia Surg, Gynec and Obstet, 20, 680, 1915
- ² Finsterer, Hans Zur Technik der paravertebralen Leitungs anathesie Zentralbl f Chir, 18, 601, 1912
- ³ Edkins Brit Jour Phys, 34, 133, 1906
- ⁴ Popielski Pfluger's Arch, 178, 214, 327, 1920
- ⁵ Ivy, A C, and Oberhelman, H A Presence of Gastrin in Human Postmortem Pyloric and Duodenal Mucosa Amer Jour Phys, 66, 451, 1923
- ⁶ Koch, P C, Luckhardt, A B, and Keeton, R W Gastrin Studies, Chemical Studies on Gastrin Bodies Amer Jour Phys, 52, 508, 1920
- ⁷ McHenry and Best Jour Phys, 67, 256, 1930
- ⁸ Sacks, J, Ivy, A C, Burgess, J P, Vandolah, J E Histamine as a Hormone of Gastric Secretion Amer Jour Phys, 101, 331, 1932
- ⁹ Koskowski, and Ivy, A C Amer Jour Phys, 75, 64, 1925

DISCUSSION—DR HARVEY B STONE (Baltimore) All of my own cases in the group which Doctor Rienhoff has reported were operated upon under general anesthesia I did not employ splanchnic block in any of my cases, and two of the three pneumonia deaths were among my own patients

It is largely a matter of speculation, of course, as to what might have been the result in these particular patients had they been operated upon under splanchnic block rather than inhalation anesthesia, but for the sake of his presentation, I wish to acknowledge very frankly that the pneumonias were all in the group receiving inhalation anesthesia

I think there is nothing more that I have to add except to say that I have been impressed with the ease and safety of the limited resection with an antecolic Pólya type repair without the addition of an entero-enterostomy It certainly is a much simpler and less hazardous procedure than the more extensive resection

On three occasions, I have resected small carcinomata in the pyloric region of the stomach under simple abdominal wall infiltration anesthesia without either general inhalation or nerve block, and without any evidence of particular distress on the part of the patient

DR J SHELTON HORSLEY (Richmond, Va) The method of anesthesia that Doctor Rienhoff has so well described is excellent, particularly in patients who are bad risks and who are elderly I have not infrequently found that a partial gastrectomy after that type of anesthesia will result in the patient's leaving the table with practically the same pulse rate, and almost the same blood pressure, as he had when he came in If it has any tendency to fall, the blood pressure is kept up by intravenous dextrose and Ringer's solution

The excision of the pyloric end of the stomach does take away, as Doctor Rienhoff has said, a kind of hormone which Edkins described, in 1906, as being produced in the pyloric portion of the stomach It seems to activate the rest of the stomach The pyloric end of the stomach, however, secretes alkaline material and not acid Resection of one-half or two-thirds of the stomach, does undoubtedly remove much of the acid-bearing portion of the stomach and,

therefore, decreases the manufacture of acid for a while but probably not permanently. For instance, if one reasonably healthy kidney is removed as the result of trauma, there may be some temporary strain upon the other kidney, but sooner or later the other kidney takes up the whole function and carries on just as well as if there were two kidneys. Similarly, sooner or later, after an extensive gastrectomy, the rest of the stomach doubtless secretes as much acid as the whole stomach did before.

Doctor Rienhoff, as is his habit, presented this so well, and his pictures are so beautiful, that it would seem almost brutal to say a word of adverse criticism, and yet I cannot refrain from remarking two or three things. One is that a Billroth I type of operation, as I tried to demonstrate this morning, preserves the physiologic function more nearly than the Billroth II type. The sensitivity of the intestinal mucosa to acid increases below the duodenum. Two or three feet below the origin of the jejunum is a region of bowel that is much more likely to be affected by the acid pouring into it than the duodenum.

The closure of the duodenum not infrequently results in back pressure, and occasionally in a duodenal fistula, which would be difficult if not impossible when the Billroth I modification is performed.

Still another criticism is that when the wound in the pancreas is left after shaving off pancreas with a knife, instead of the cautery—the cautery seals it and makes it sterile and kills some of the infective agents—the pancreas is left exposed and unprotected whereas, when it is cut with a cautery and the Billroth I modification described this morning, is employed, the stomach is brought over to the stump of the duodenum, united in a physiologic way, and the wounded surface of the pancreas is covered by the posterior wall of the stomach.

DR FRANK H. LAHEY (Boston). After having had a fatality from a cyclopropane explosion, we interested the Massachusetts Institute of Technology in trying to find out what caused the explosion and to develop something which will probably diminish the likelihood of such explosions. This is only one thing toward reducing explosion hazards, but I would feel wrong if I went home without presenting the plan of this intercoupler which has been devised.

This work has been done by Professor J. W. Horton, Professor of Biological Engineering at the Massachusetts Institute of Technology, in cooperation with the members of the Department of Anesthesia of the clinic.

This intercoupler unit provides a means for electrically intercoupling the patient, the anesthetist, the machine, and the operating table. It thus keeps them all at the same electrical potential. Its purpose is to eliminate static spark between any two of these bodies and thus reduce the hazard of igniting explosive anesthetic agents. You all know the value of ordinary intercoupling in reducing static. This is, however, a new type of intercoupler. It has five segments to it, and each segment has in it a resistance of one million ohms, that is, one megohm. This resistance of one million ohms is introduced into the connection between each pair of intercoupled bodies, making it possible to intercouple five units—table, anesthetist, apparatus, anything else, five individuals can be intercoupled with a resistance of one million ohms between each one. In this way certain risks which would accompany direct intercoupling by ordinary chains or wires are avoided. Any current from the lighting circuit which might accidentally pass to the patient or anesthetist through the intercoupling connection is limited to magnitudes which are not dangerous.

The intercoupled bodies are also prevented (this is the important development, I think) from acting as a single electrostatic condenser of high capacity.

This is desirable in order not to increase the energy in any sparks which may be received from uncoupled bodies. It must be emphasized that the sole function of the intercoupler is to equalize electrostatic potentials between such bodies as may be directly connected to it. It provides no immunity from electrostatic discharges from other bodies. Its use does not justify the neglect of any other possible precaution against electrostatic sparks or against other agents which may ignite inflammable gases.

We do not sell it, we are not interested in it. It is built by the hospital. It costs but \$7.50. It is very definitely a method by which sparks built up in a unit, which is part of the operation, can be reduced to such a degree of heat that they will not ignite inflammable gases. This is of particular importance, since most of the explosions will occur from leakages about the face mask or from within the apparatus itself.

I do not think this is the complete answer to the prevention of explosions. It is, however, a distinct aid in preventing explosions from their common cause, that is, charges built up within individuals or within apparatus and the production of static sparks particularly close to the mouthpiece.

DR ROSCOE GRAHAM (Toronto, Canada). I should like to present certain facts in regard to our impressions of spinal anesthesia in abdominal surgery. Conflicting reports, conflicting enthusiasms, and the unfortunate sequelae that have been reported would seem sufficient to condemn spinal anesthesia. Despite the fact that these reports have been published, the preference of our staff for spinal anesthesia in upper abdominal lesions is represented by 144 instances in 158 recent upper abdominal operations.

I think that the conflict of practice and report is probably due to the fact that many statements are passed on without substantiation. Doctor Foss' case is an excellent example of where an entirely irrelevant lesion is blamed on the anesthetic. We believe that the adequate operation which can be performed under spinal anesthesia is a great advance. Your experience may be at variance with ours, but in the question of common bile duct lesions, prior to January, 1934, we never did find more than a 10 per cent occurrence of stones in the common bile duct in conjunction with cholelithiasis. There was a reason. We opened the common bile duct only in cases where it was obviously impaired, because the trauma, resultant morbidity, and the disturbed convalescence deterred us.

Our interest in modifying the ordinary inhalation anesthesia started in 1926. At this time, we adopted splanchnic block through the open abdomen as advocated by Doctor Finsterer and presented to you to-day by Doctor Rienhoff. I think it was good for the patient. It was hard on the surgeon, and in 1930, we supplanted this by the use of spinal anesthesia.

In the last 311 cases of cholelithiasis, we have explored the common duct in 46 per cent of cases and we have removed stones in 21 per cent. That is a sad comment on our ability as surgeons previously, but it is an excellent commendation of our belief that with the relaxation of spinal anesthesia in these complicated and difficult intraperitoneal operations, we can carry out this type of operative and technical procedure with full confidence that that procedure is not adding to the mortality and morbidity. Furthermore, we believe that the conflict of opinion and practice with regard to spinal anesthesia is due to three factors. First the choice of the anesthetic agent, and second, the anesthetist. We have never used an anesthetic agent that was not dependent for the height of anesthesia on the volume of fluid injected. We use procaine or novocain, either in crystal form or in solution, or nupercain in 1:1500 dilution.

We have never had a serious neurologic lesion. We had one which was discovered only on the day following operation, and that was the paresis of the external rectus muscle of the eye. It seems difficult to understand that such could be due to the spinal anesthesia, but it has been reported by others. It cleared entirely in three weeks.

The third important factor we believe is the method and the technic of administration. We most heartily must condemn the surgeon who is his own anesthetist and uses spinal anesthesia. We believe that spinal anesthesia, unless administered and supervised by a skillful and adequately trained anesthetist, is a dangerous anesthetic. We believe that we must correct biochemical faults and fluid imbalance before administering spinal anesthesia. We further believe that the use of small needles, No. 22 gauge, is of importance in preventing postoperative spinal headaches. In addition, the elevation of the foot of the bed ten inches for ten hours and the intravenous administration by the drip method of 1,500 to 2,000 cc. of saline postoperatively we believe is of importance in preventing spinal headache.

The freedom from complications with spinal anesthesia is outstanding in our experience when compared with a similar group of operations carried out under inhalation anesthesia.

Many of the condemnations of spinal anesthesia are because it is not of sufficient duration to permit prolonged and complicated intraperitoneal operations. That is true, technically, in the cases such as were described this morning of the gastrojejunal fistulae which are particularly difficult and require prolonged procedures.

The supplemental inhalation anesthesia, particularly if the patient has been given adequate preoperative sedation, we feel is accompanied by real handicap. We had one patient who died, we believe, of anoxemia and fulfilled the requirements which Doctor McClure and Doctor Hartman presented. The patient had been given major sedation previous to operation, and that had been supplemented during the operation by intravenous sodium amytal to control the nausea. Following the supplemental inhalation anesthesia, the patient developed apnea for some time, with the resultant anoxia. The patient died seven hours later.

If the duration of the operative procedure is such that it is likely to require supplemental anesthesia, we do not give excessive sedation, and we do not supplement with deep inhalation anesthesia, but anticipating the diminution of the efficacy of our spinal anesthesia, we use splanchnic block at this time coupled with field block. That has been most efficacious, and I would only ask, in conclusion, that we recognize the limitations of spinal anesthesia, that we recognize it as a dangerous anesthesia unless there is adequate preparation, skillful support, supervision and administration of the anesthesia, that we hesitate to pass on criticisms and statements of sequelae without first substantiating them by fact.

DR FRASER B. GURD (Montreal, Canada). I feel that it is necessary, or at least advisable, on my part to indicate the reason why, three years ago, we were induced to commence the employment of spinal anesthesia for thoracoplasty in the treatment of pulmonary tuberculosis.

About 50 years ago, there was established in Montreal the Grace Dart Home. The establishment of this home was in order that cases about to die from pulmonary tuberculosis could be, in the first place, removed from their homes, and in the second place, made as comfortable as possible. In 1932, a hospital was built to replace the home. Nevertheless, the traditions of the old Grace Dart Home continued, and to the new hospital was admitted, in large

measure, the same type of cases. An operating room had been provided in the new hospital, and, in 1933, I was asked to organize a surgical staff for the purpose of employing surgical therapy in the treatment of the cases.

Our medical staff, that is, the physicians proper, put the matter up to me in this way, stating that "We are all familiar with the results of thoracoplasty in the properly selected cases according to Doctor Archibald's good, chronic type. Will you be willing to undertake surgical interference in the type of cases we have in this hospital in order to discover whether these cases, or some of these cases, who appear to be destined to early exitus cannot have the course of the disease arrested?"

Having worked for three years in France at a Clearing Station, and having under those conditions had thousands of young men die under my care, I replied that I was quite prepared to carry out such a form of treatment.

During the first two or three years (the service, by the way, is not a large one), there were 27 cases operated upon, that is, about 100 operations. We employed all forms of anesthesia and all mixtures of anesthetics, including cyclopropane, evipal, avertin, ether, nitrous oxide, and various forms of pre-operative sedation. Of the 27 cases operated upon prior to July, 1936, we had seven deaths within six weeks of operation, that is, we had seven which we considered postoperative deaths. I felt it was necessary, having such a mortality rate, to state my apologia before stating the figures.

Four of those deaths were frankly due to bronchial spreads of the disease, and the postoperative institution of an acute pneumonic phthisis. In addition, there were eight other cases in which extensive and marked bronchial spreads occurred. Those patients ultimately died, and more quickly, we are sure, than had they not been operated upon.

We were depressed, and spoke to Doctor Bourne, who has spoken to us here this afternoon, and asked him whether he thought we could try some other method, especially spinal anesthesia, in the hope that in this particular type of case we might be able to improve our results.

I am going to state the matter very briefly from here, gentlemen. Since July, 1936, we have operated upon 42 cases, 24 of whom were bilateral. We have had two deaths in the operating room. We have had three commotions, I would call them, that is, in three cases we were disturbed in the operating room by the condition of the patient. The patients, however, afterwards did well. There have been three minor spreads. We have had no deaths other than the two in the operating room during the first two months following operation.

Of those 42 cases, 37 were extrapleural thoracoplasties, usually three-stage, commencing with the third, second and first ribs, and five were the production of extrapleural pneumothoraces which, as you know, necessitates, among other things, the dissection of the extrafascial plane of the thorax from the brachial plexus and the subclavian vessels.

In no case have we had to supplement with any other anesthetic. In no case has there been any complaint or special apprehension on the part of the patient who had to undergo a second and then a third operative procedure. In but two cases have we deemed it expedient to employ blood transfusion, although as a matter of fact we are in a position to employ blood transfusions easily, but we have not thought it necessary.

We have employed the Etherington-Wilson technic, which is that, in the erect posture, from 12 to 13 cc of nupercain (1:1,500) is introduced between the second and third lumbar interspace. The back of the patient has been estimated as being long, short or medium in length. We have, or rather Doctor Bourne has, following the commencement of the introduction of the

hypotonic, that is, hypotonic as compared to the cerebrospinal fluid, started the stop-watch, and from 50 to 55 seconds has been the length of time which we have deemed was the proper length of time to reach the sixth cervical region, approximately

That, briefly, gentlemen, is our statement. As I said in the first place, we explained as to why we felt justified in carrying out the experiment. Our experiment, if such it may be called, and I think it can be properly called so, is justified by our results, and in any event it proves quite conclusively that with comparative safety, and with certain satisfaction to both surgeon and the patient, the first rib together with its transverse process may be removed in its entirety, and as I have already pointed out, that necessitates the displacement of the whole of the brachial plexus, since we make it a practice to carry out substantially Semb's procedure without undue mortality. We are not certain why the two patients died in the operating room. We are prepared to admit that they were due to our form of anesthesia, although that is not positively certain in our own minds.

DR ERWIN R. SCHMIDT (Madison, Wis.) The discussion this afternoon has raised certain questions in my mind. In the discussion on anoxia, I am not worried so much about the people that died, because they are evidently taken care of, but I am wondering about the many people who have been crippled by different degrees of anoxia of which we know very little. It certainly is a subject over which we as surgeons should very carefully cogitate.

With reference to the explosions, having been one of the individuals who helped bring cyclopropane into the surgical field, there are certain questions that come up in my mind. In the first place, several years have elapsed, and cyclopropane has been used, and it is only recently that the explosions have happened. That is one question.

Then, as far as the statistics are concerned, I do not believe much in statistics any more. At the present time we are getting some reports of explosions, but as far as I know, ever since the discovery of anesthesia—ether and chloroform—we have had several agents at our disposal, and of all the agents, only local and chloroform are nonexplosive agents. It is my personal opinion that we know very little of what is happening in the field of anesthesia, because only within the last few years have we had people who knew something about anesthesia, and these individuals are interested in reporting what they have found, a real search after the truth. Before this time, I have a feeling that a great many explosions are buried in the memories of men.

We come to realize that there are many agents, and it seems to me as surgeons we have to realize that it requires a great deal of knowledge in many different ways in order to bring the information which we have to focus on the problems we have with each individual patient. I agree very heartily with Doctor Graham, when he discussed spinal anesthesia, that it is only within the last few years that we are really obtaining some evidence that we can depend upon in determining the clinical course, or the things we want to do with patients as far as anesthesia is concerned.

Now, it seems to me that viewing this with a general, broad viewpoint, it sums itself up something like this. What may be a good anesthesia in my hospital is not a good anesthesia in your hospital, and if we recognize that and use some common sense in the agents that we employ, so that in each individual place the agent, whatever it may be, is the best one that can be employed in that individual place, then I think we will find a great improvement in our anesthesia, and I believe that the enthusiasm, the work and the science that have been applied by this small group of individuals, are going to amplify the art which has been practiced so many years in surgery and anesthesia.

THE SIGNIFICANCE OF LIPOCAIC IN SURGERY*†

LESTER R. DRAGSTEDT, M D , P H D , DWIGHT E. CLARK, M D

AND

C. VERMEULEN, M D

CHICAGO, ILL

FROM THE DEPARTMENT OF SURGERY OF THE UNIVERSITY OF CHICAGO, CHICAGO, ILL

TWO YEARS after the isolation of insulin by Banting and Best,¹ in 1922, it was discovered by Fisher² and by Allan, Bowie, Macleod, and Robinson³ that completely depancreatized dogs could not be kept alive for long, even though adequately treated with the new hormone. Death usually took place within two or three months. At autopsy, the liver was found to be markedly enlarged and its parenchyma almost entirely replaced by fat (Figs. 1 and 2). The addition of raw pancreas to the diet was found by Macleod and his associates to prevent the development of these liver changes and to permit survival for long periods of time. These findings have been repeatedly confirmed. In 1930, Hershey,⁴ and, in 1931, Hershey and Soskin,⁵ reported that the addition of 10 Gm of lecithin daily to the diet of the depancreatized dog treated with insulin was also effective in preventing the characteristic liver damage and in permitting survival. The active constituent in this effect was found by Best and Huntsman,⁶ and Best, Ferguson, and Hershey⁷ to be choline.

The depancreatized animal suffers from two obvious deficiencies—insulin and pancreatic juice. The fact that insulin, together with an adequate, balanced diet, does not suffice to permit such animals to survive in good health suggested that the pancreatic secretion might also be necessary. In fact, it was this possibility that led Macleod and his associates to investigate the effect of feeding raw pancreas as a source of the pancreatic enzymes. The discovery that lecithin and choline were, at least to some extent, effective in preventing the liver changes in depancreatized dogs cast doubt on the assumption that pancreatic juice or certain of its constituents were necessary, and it was perhaps fairly generally believed that the beneficial effect of pancreas feeding was due to its content of lecithin and choline.

During the past four years, a considerable amount of evidence has been accumulated in our laboratory^{8, 9, 10} which indicates that neither of these assumptions is correct. On the other hand, the conclusion seems inescapable that the pancreas manufactures a second internal secretion, apart from insulin.

* This work has been aided by grants from the Josiah Macy, Jr., Foundation, the Committee on Research in Endocrinology of the National Research Council, the Douglass Smith Foundation for Medical Research of the University of Chicago, and the Eli Lilly Co.

† Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

which plays an important and perhaps vital rôle in metabolism. This evidence may be in part summarized as follows:

(a) The failure of the insulin treated depancreatized dog to survive is

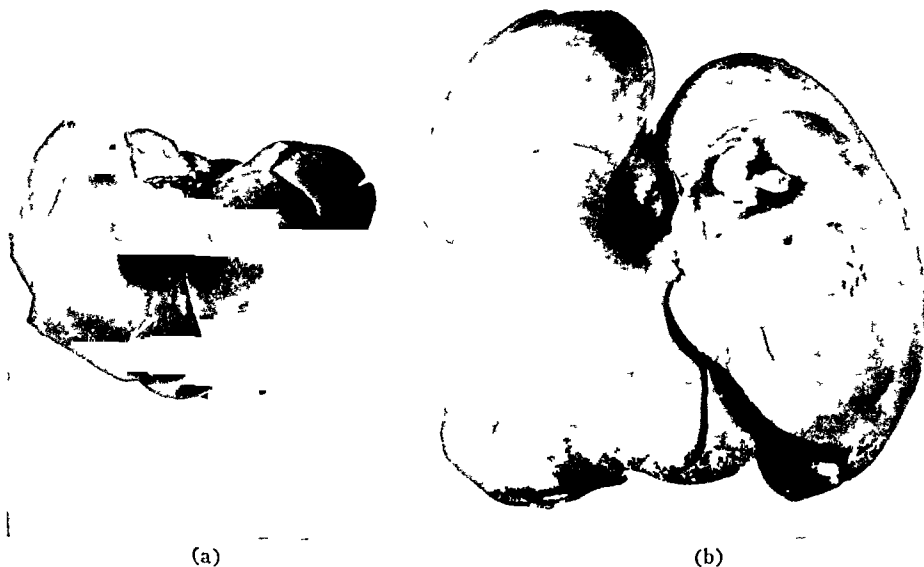


FIG 1—(a) Photograph of normal liver of dog. (b) Photograph of the liver of an animal of approximately the same size, that had been depancreatized and preserved as long as possible by the administration of insulin. Death occurred after 60 days and, at autopsy, the liver was found to be enlarged and bright yellow in color.

not due to the absence of pancreatic juice or its constituent enzymes, since animals with complete pancreatic fistulae may survive indefinitely if demineral-

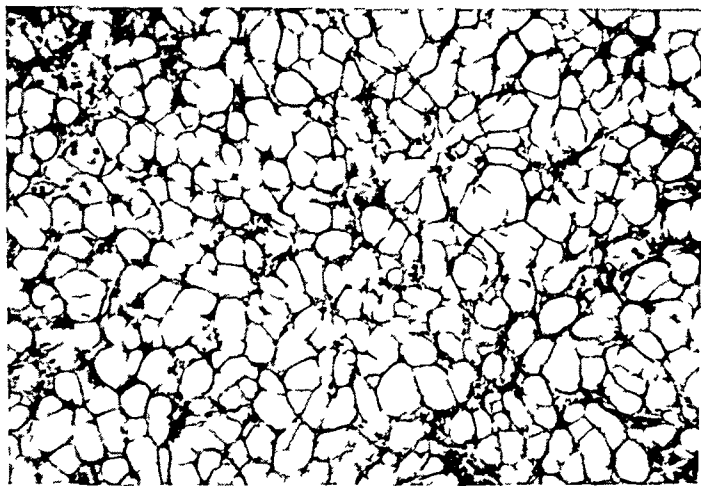


FIG 2—Photomicrograph showing the marked fatty infiltration of the liver in a depancreatized dog fed a balanced diet and treated adequately with insulin. Death occurred 60 days after pancreatectomy.

alization and the development of ulcers in the stomach and duodenum are prevented.^{11, 12, 8} Such animals do not develop the fatty changes in the liver which appear in insulin treated depancreatized dogs. Furthermore, the oral administration of fresh active pancreatic juice does not prevent the development of fatty infiltration of the liver in depancreatized dogs nor prolong life

As a matter of fact, the fatty infiltration occurred somewhat sooner and was more marked in these animals than in the control group that received no pancreatic juice. This is probably to be attributed to the better digestion and absorption of fat in the former case.

(b) The beneficial effect of pancreas feeding in preventing the fatty infiltration of the liver in insulin treated depancreatized dogs is not due to its content of lecithin or choline, since liver and brain, which contain even more of these substances, have no such beneficial effect.⁸ If depancreatized dogs are fed a mixed diet of protein, carbohydrate, and fat and the diabetes is well controlled by insulin, it requires at least 20 Gm of choline over and above that which is present in the food in order to prevent the characteristic fatty changes in the liver. One hundred Gm of fresh pancreas, which is an adequate preventive or curative dose, contains only 232 mg of choline.¹³

(c) It has been possible to prepare extracts of pancreas that are entirely free from lecithin and practically free of choline and which are just as effective as raw pancreas in preventing or curing the fatty changes in the livers of depancreatized dogs and in permitting these animals to survive. The details of the method of extraction will be presented elsewhere. It may be stated here that fresh beef pancreas is first thoroughly extracted with neutral alcohol. The filtrate may then be evaporated to dryness and extracted with ether. The ether extract contains the fat of the pancreas and hence practically all the lecithin and choline, but has no therapeutic value. The fat-free alcohol extract is, however, effective on oral administration in amounts of from 1 to 2 Gm per day in preventing and curing fatty infiltration of the liver in depancreatized dogs. Figure 3, a, b, c, d, e and f, illustrates the improvement in the histologic appearance of the liver brought about by this material. This fat-free alcohol extract may be further concentrated and purified by dissolving it in water and then precipitating it out by saturation with ammonium sulphate. The precipitate may be then dissolved in glacial acetic acid. The addition of ether to the glacial acetic acid throws out a precipitate which has been found to be active by both oral and subcutaneous administration in amounts of less than 150 mg per day. This product contains no fat and is free of appreciable amounts of choline.

The demonstration that a second internal secretion is normally provided by the pancreas depends upon the recognition that the depancreatized dog, fed upon a mixed diet of protein, carbohydrate, and fat is not restored to a normal state by the adequate administration of insulin and pancreatic juice, and that the remaining deficiency can be corrected by the oral administration of pancreas or of certain extracts of pancreas, but not by other organs. We have suggested the name "lipocaic" for this hormone. This is derived from the Greek and suggests in a general way the oxidation of fat. The function of this internal secretion is still very little understood. The sequence of events which commonly follows when a dog is pancreatectomized and thus deprived of pancreatic secretion, insulin and lipocaic is as follows: Hyperglycemia, hyperlipemia, glycosuria, disturbance in digestion, increasing emaciation.

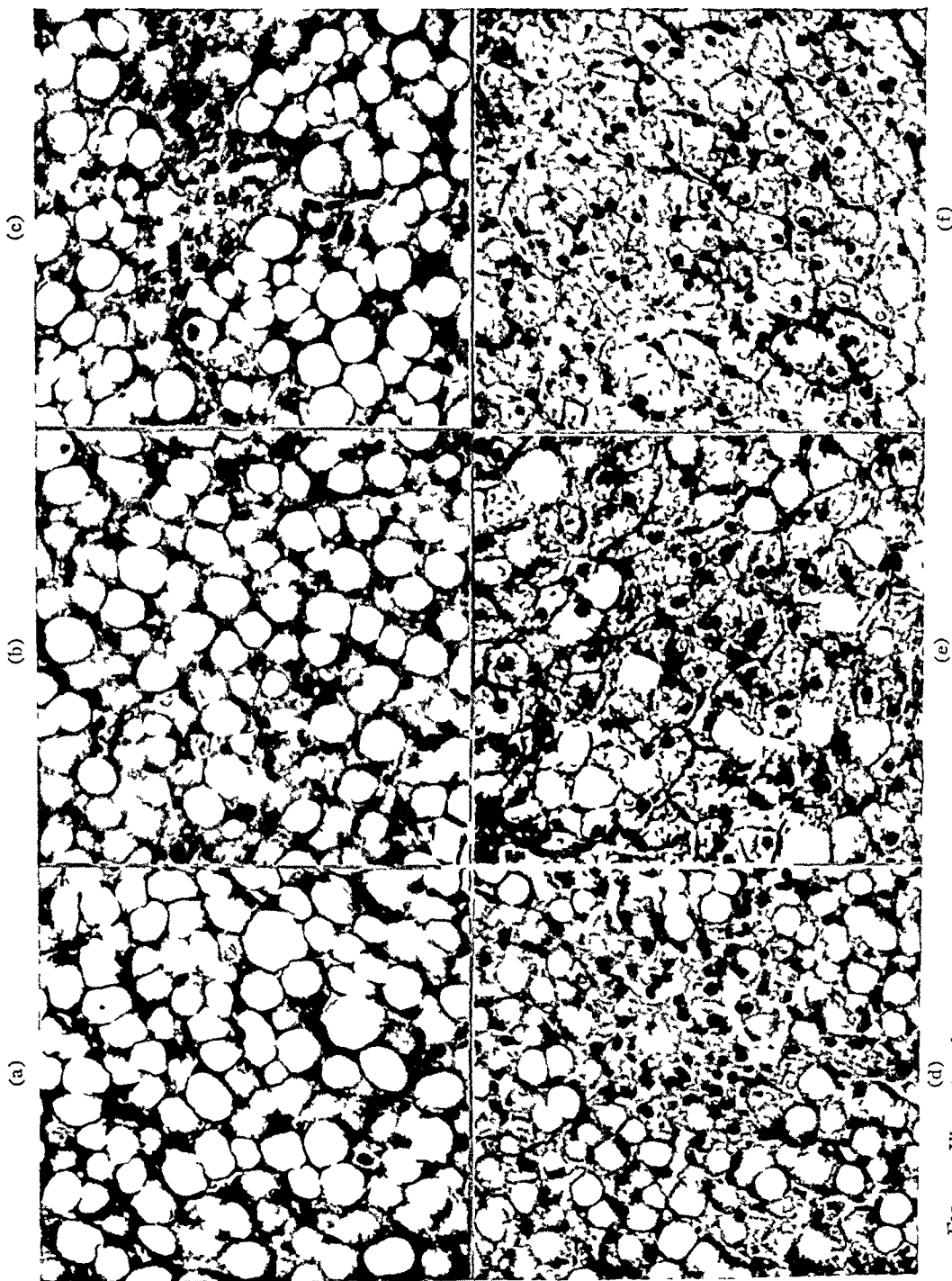


FIG 3.—Illustrates the improvement in the histologic appearance of the liver produced by the oral administration of lipocac (1) Dog 665 Biopsy showing extensive fatty infiltration in the liver ten weeks after pancreatectomy. Liver function test showed 30 per cent retention of bromsulphalein 20 minutes after injection of the dye (b) Dog 665 Biopsy of liver after oral administration of 1.0 Gm of fat free alcohol extract of pancreas daily for two weeks. There is no decrease in fat but the liver function test was now normal (c) Dog 665 Biopsy of liver after oral administration of lipocac for four weeks. There is some decrease in fat and a small island of normal liver tissue. Liver function normal (d) Dog 665 Biopsy of liver after oral administration of lipocac for six weeks. There is still more decrease in the liver fat (e) Dog 665 Biopsy of liver after eight weeks of lipocac therapy showing marked improvement (f) Dog 665 Biopsy of liver after 12 weeks of lipocac therapy, showing almost complete return of normal structure

ciation, and death from so-called pancreatic diabetes in one to four weeks. If this depancreatized animal be placed on a mixed diet of protein, carbohydrate, and fat, given active pancreatic juice by mouth, and sufficient insulin (usually 10 to 20 units) to limit the excretion of urinary sugar to about 10 Gm per day, life is considerably prolonged and the defect due to the absence of lipocaic made manifest.

There occurs a steadily lessening excretion of glucose in spite of continually decreasing doses of insulin, until after five or six weeks the animal may excrete only a gram or two of glucose per day and receive only two or three units of insulin. Larger amounts, even five units, may at this time provoke fatal hypoglycemic convulsions. Superficially, it might appear as though the animal were recovering from the diabetes. However, certain definite abnormalities are present. The blood fats are reduced to approximately one-half of the normal concentration and tests reveal defective liver function. An abnormal retention of bromsulphalein¹⁴ is commonly found. Whereas digestion and absorption are improved by the administration of pancreatic juice, the animal becomes progressively weaker and emaciated and death occurs. At autopsy the liver is found to be enlarged to three or four times its normal size and so infiltrated with fat that its normal architecture is entirely obscured. Of 154 depancreatized dogs, whose course was carefully studied in our laboratory, only 13 failed to develop these fatty changes. Both regular and protamine-zinc insulin have been used in this work and no significant difference observed.

If lipocaic be given to such a depancreatized animal at the time when the sugar excretion has become minimal, the insulin requirement reduced, the liver function impaired, and the concentration of blood fats decreased, a striking change is produced. The blood lipids increase to normal or greater than normal values, an immediate and large excretion of glucose in the urine occurs, and the insulin dosage may be raised to 20 or 25 units per day without harm. Liver function returns to normal within two or three weeks and occasionally sooner. Biopsies of the liver during this period disclose a rapid disappearance of the fat and a return of the normal structure. The large glucose excretion and increased tolerance to insulin suggest that under the influence of lipocaic the fat in the liver is being converted into glucose. The possibility of such conversion in the organism has long been recognized for the glycerol part of the fat molecule, but denied for the fatty acid. The very large amounts of glucose made available in these experiments seem to demand such a conversion for the fatty acid. The general condition of the animal, its weight, strength, and appetite steadily improve under lipocaic administration and the diabetes reaches a steady state without fluctuations in glucose excretion or insulin requirement. The subsequent withdrawal of lipocaic again produces the characteristic symptoms and findings, which may be again relieved by lipocaic, and this process often repeated.

It seems likely that clinical application of these findings on the lower animals will be obtained chiefly in medicine. There is considerable evidence

at present which indicates that some patients with diabetes mellitus are not returned to an entirely normal state by the administration of insulin. A lessened capacity to utilize fats is often present and some students of this disease have advocated a low fat, high carbohydrate diet plus insulin in treatment. Enlargement of the liver due to extensive fatty infiltration has been reported and several of these cases have responded favorably to lipocaic administration.

Grayzel and Radwin¹⁵ treated three young diabetics with hepatomegaly by means of lipocaic and secured a striking recession of the liver to its normal size. When the lipocaic was discontinued, the hepatomegaly returned and again receded when lipocaic was resumed. The diabetes in these pa-

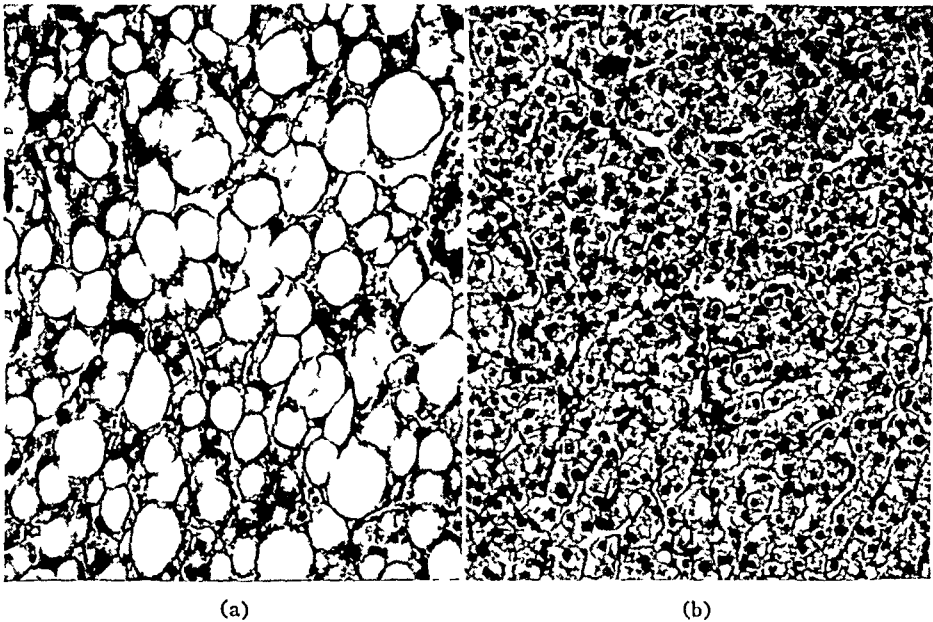


FIG 4 —(a) Biopsy showing marked fatty metamorphosis of the liver in Rosenberg's case. (b) Second biopsy showing the marked improvement in the liver produced by the oral administration of lipocaic.

tients had been well controlled by diet and insulin. The case reported by Rosenberg¹⁶ is of special significance, since it was possible to verify the diagnosis of fatty metamorphosis of the liver at operation and to secure a biopsy specimen, and again to verify the improvement brought about by lipocaic at a second operation. The case was that of a woman, age 59, with mild diabetes, hepatomegaly, and laboratory evidence of impaired liver function. Celiotomy was performed for the removal of an ovarian tumor and at this time the liver was found to be enlarged and grossly fatty. Figure 4a, obtained through the courtesy of Doctor Rosenberg, illustrates the almost complete replacement of the hepatic parenchyma by fat. Lipocaic was then administered orally for a period of 11 weeks, during which time there was marked subjective improvement, decrease in the size of the liver, and improvement in its function as determined by the bromsulphalein and hippuric acid tests. An attack of biliary colic during the twelfth week necessitated a second operation and at this time the author reported a remarkable change in the size and appearance of the liver, which was now normal. A second

biopsy (Fig 4b) revealed a complete disappearance of the fat and return of the normal histologic structure

The surgeon will perhaps see cases of fatty metamorphosis of the liver due to lipocaic deficiency where the pancreas has been extensively destroyed following attacks of acute pancreatitis or pancreatic necrosis or where the pancreas has been extensively removed in the treatment of malignant disease. We are indebted to Dr Warren Cole for Figure 5, which illustrates the extreme fatty metamorphosis in the liver in a patient who, at autopsy, displayed an almost complete destruction of the pancreas, probably as a result of repeated attacks of acute pancreatitis. The development by Whipple, Parsons, and Mullins¹⁷ of a technic for extirpation of carcinoma of the ampulla and

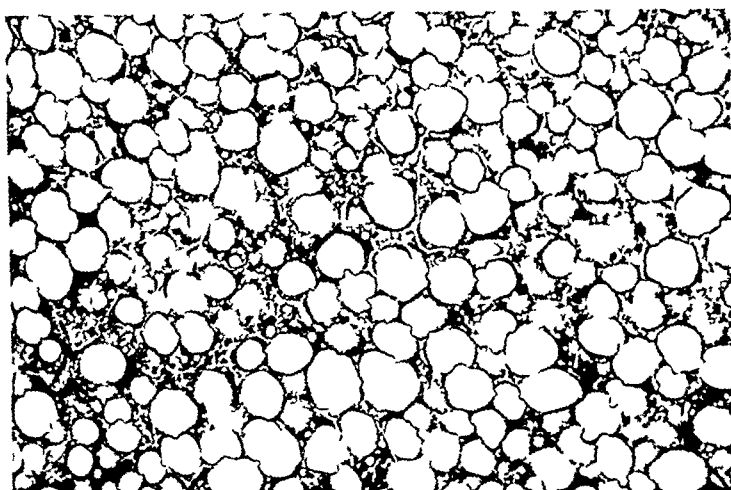


FIG 5 —Photomicrograph showing the extensive fatty metamorphosis of the liver in Warren Cole's case

of the pancreas seems destined to become increasingly successful, and we will doubtless see more and more long-time survivals following such operations. We have no reason to believe that the response of man to pancreatectomy will be different from that in the dog. In that case, it seems important to recognize that the absence of pancreatic juice from the intestine is relatively unimportant, leading only to a partial impairment in digestion and absorption, whereas the deficiency in the internal secretions, insulin and lipocaic, is incompatible with life.

REFERENCES

- ¹ Best, C H, and Banting, F G. Internal Secretion of Pancreas. *J Lab and Clin Med*, 7, 251-266, February, 1922.
- ² Fisher, N F. Attempts to Maintain Life of Totally Pancreatectomized Dog Indefinitely by Insulin. *Am J Physiol*, 67, 634-643, February, 1924.
- ³ Allan, F N, Bowie, J J, Macleod, J J R, and Robinson, W L. Behaviour of Depancreatized Dogs Kept Alive with Insulin. *Brit J Exper Path*, 5, 75-83, April, 1924.
- ⁴ Hershey, J M. Substitution of Lecithin for Raw Pancreas in Diet of Depancreatized Dog. *Am J Physiol* 93, 657, June, 1930.
- ⁵ Hershey, J M, and Soskin, S. Substitution of "Lecithin" for Raw Pancreas in Diet of Depancreatized Dog. *Am J Physiol*, 98, 74, August, 1931.

- ⁶ Best, C H, and Huntsman, M J Effects of Components of Lecithin upon Deposition of Fat in Liver J Physiol, 75, 405-412, August, 1932
- ⁷ Best, C H, Ferguson, G C, and Hershey, J M Choline and Liver Fat in Diabetic Dogs J Physiol, 79, 94-102, July 28, 1933
- ⁸ Van Prohaska, J, Dragstedt, L R, and Harms, H P The Relation of Pancreatic Juice to the Fatty Infiltration and Degeneration of the Liver in the Depancreatized Dog Am J Physiol, 117, 166, September, 1936
- ⁹ Dragstedt, L R, Van Prohaska, J, and Harms, H P Observations on a Substance in Pancreas (a Fat Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatized Dogs Am J Physiol, 117, 175, September, 1936
- ¹⁰ Dragstedt, L R, Vermeulen, C, Goodpasture, W C, Donovan, P B, and Geer, W A Lipocic and Fatty Infiltration of the Liver in Pancreatic Diabetes Arch Int Med, in press
- ¹¹ Dragstedt, L R, Montgomery, M L, and Ellis, J C A New Type of Pancreatic Fistula Proc Soc Exper Biol and Med, 28, 109, 1930
- ¹² Harms, H P, Van Prohaska, J, and Dragstedt, L R The Relation of Pancreatic Juice to Pancreatic Diabetes Am J Physiol, 117, 160, 1936
- ¹³ Fletcher, J P, Best, C H, and Solandt, O M Biochem J, 29, 10, 1935
- ¹⁴ Goodpasture, W C, Vermeulen, C, Donovan, P B, and Dragstedt, L R The Bromsulphalein Liver Function Test as a Method of Assay of Lipocic Am J Physiol, 124, 642, 1938
- ¹⁵ Grayzel, H G, and Radwin, L S Am J Dis Child, 56, 22, 1938
- ¹⁶ Rosenberg, D H A Proved Case of Recovery from Fatty Metamorphosis of the Liver after Treatment with Lipocic Am J Digest Dis, 5, 607, 1938
- ¹⁷ Whipple, A O, Parsons, W B, and Mullins, C R ANNALS OF SURGERY, 102, 763, 1935

DISCUSSION—DR J SHELTON HORSLEY (Richmond, Va) This is a remarkably interesting paper, not only for the discovery of an apparently new histogenesis of fatty changes in the liver, but because it opens up several other questions. One, for instance, is that in the so-called fatty degeneration of the liver after certain drugs, such as chloroform, which is a well-known cause of death after chloroform anesthesia, may it not be possible that this fatty degeneration is not due to a direct effect upon the hepatic cells, but to the action upon the pancreas, which in turn produces this fatty degeneration of the liver by a suppression of lipocic? I should like very much to hear Doctor Dragstedt express his opinion about this.

A quite dramatic thing is the recovery of a liver that seems to be practically all fat. I am wondering if those areas of fat are true fat cells—they can hardly be—or whether it is just an accumulation of fat within the capsule of the cell. It would seem remarkable that a portion of a liver apparently consisting of nothing but fat, like a lipoma, could regenerate so completely under lipocic, and hepatic cells be built up from what seem masses of fat. There doubtless must be some element of nucleus or something else in the capsule of these fat-like cells that initiates regeneration.

DR FREDERICK REICHERT (San Francisco) I should like to ask Doctor Dragstedt if he knows whether this second internal secretion of the pancreas is affected by hypophysectomy. As I remember the study of the livers in hypophysectomized young animals, they appeared normal, but I do not recall the appearance of the liver in adult dogs.

DR LESTER R DRAGSTEDT (closing) Doctors Bollman and Mann have recently made some significant studies with respect to the nature of the fatty livers which occur following the administration of alcohol. They found that

if dogs were placed on a diet deficient in carbohydrate but rich in fat, and then given alcohol, an extreme fatty infiltration in the liver develops. This fatty infiltration could be relieved by the administration of carbohydrate and also to a certain extent by the administration of lipocaic.

Doctor Horsely's question presents a very interesting suggestion. It is indeed possible that the fatty infiltration of the liver that follows upon the administration of alcohol might well be due to inhibition of the formation of lipocaic by the pancreas. The fat in these cases is in the hepatic rather than the Kupffer cells. The very large amount of fat present gives the cell a signet-ring appearance. Animals that have survived for long periods of time with only moderate degrees of fatty infiltration display a very marked cirrhosis of the liver.

In answer to Doctor Reichert's question, fatty infiltration in the liver does not regularly develop in the hypophysectomized animal. However, if the hypophysis is removed and then at a subsequent date a total pancreatectomy is performed, a mild type of diabetes develops, as was demonstrated by Houssay, and these animals develop a marked fatty infiltration in the liver, similar to that which occurs in the depancreatized dog. This type of fatty liver in the Houssay dog is also relieved by the administration of lipocaic.

A DISCUSSION OF MULTIPLE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE)*

REPORT OF TWO CASES HAVING UNUSUAL SURGICAL COMPLICATIONS

RANDOLPH JONES, JR., M D

AND

DERYL HART, M D

DURHAM, N C

FROM THE DEPARTMENT OF SURGERY OF THE DUKE UNIVERSITY SCHOOL OF MEDICINE, DURHAM, N C

MULTIPLE NEUROFIBROMATOSIS remains a disease of great interest because of the probable familial nature of the affection, the complexity of its morphology, the progressive character of its course, and the numerous complications which may develop during its evolution. Moreover, although von Recklinghausen's disease has been the object of study by many investigators, there is still some lack of agreement in the interpretation of certain of its aspects, and the cause of the disease remains unknown. In this presentation we will make a general survey of the disease, with illustrations of its familial character and many of its clinical manifestations, taken from our own records. Two of our cases with unusual complications, requiring surgical intervention, are reported in detail.

The Familial Character of von Recklinghausen's Disease—That multiple neurofibromatosis frequently recurs in successive generations of the same family has long been known, but the hereditary character of the disease did not attract widespread attention until 1910.¹ In its hereditary occurrence, it is analogous to multiple telangiectasis,[†] to tuberous sclerosis, and to polyadenomata of the rectum.² Although it is not possible in all cases to demonstrate inheritance of the condition, the percentage of patients having a family history of the disease varies in different reports from 18 to 74 per cent.³

It is also of interest to note that similar clinical types of the affection may appear in several individuals of the same or successive generations of a given family,⁴ as has been reported in uniovular twins,⁵ in a family with intracranial tumors in a high percentage of members through three generations,⁶ and in other families showing a high incidence of malignancy.⁷

Numerous instances of the transmission of multiple neurofibromatosis through three generations are on record.^{4,8} A number of our patients have given a family history of the disease, and in one we have been able to trace it through four generations while the members of the fifth are too young as yet to show definite signs of involvement (Chart 1). Although there is some doubt that the hereditary factor is transmitted as a mendelian dominant, such

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

† Hemangiomatosis is mentioned also as an hereditary disease affecting the central nervous system.⁸

seems to have been the case in a number of families which were followed for more than two generations,^{4, 9, 10} and this view is supported by the family tree shown in Chart I. That the inheritance is not sex linked, is also borne out by this family (Chart I). The failure of the disease to appear in a given generation has been explained on the assumption that the condition may be transmitted in a latent or unrecognized form, or that the well phenotype may be the carrier of the tendency.¹ It seems highly probable that the failure of the process to be recognized in those families which have noted a disappearance of the disease in the line of inheritance for one generation (or more) may

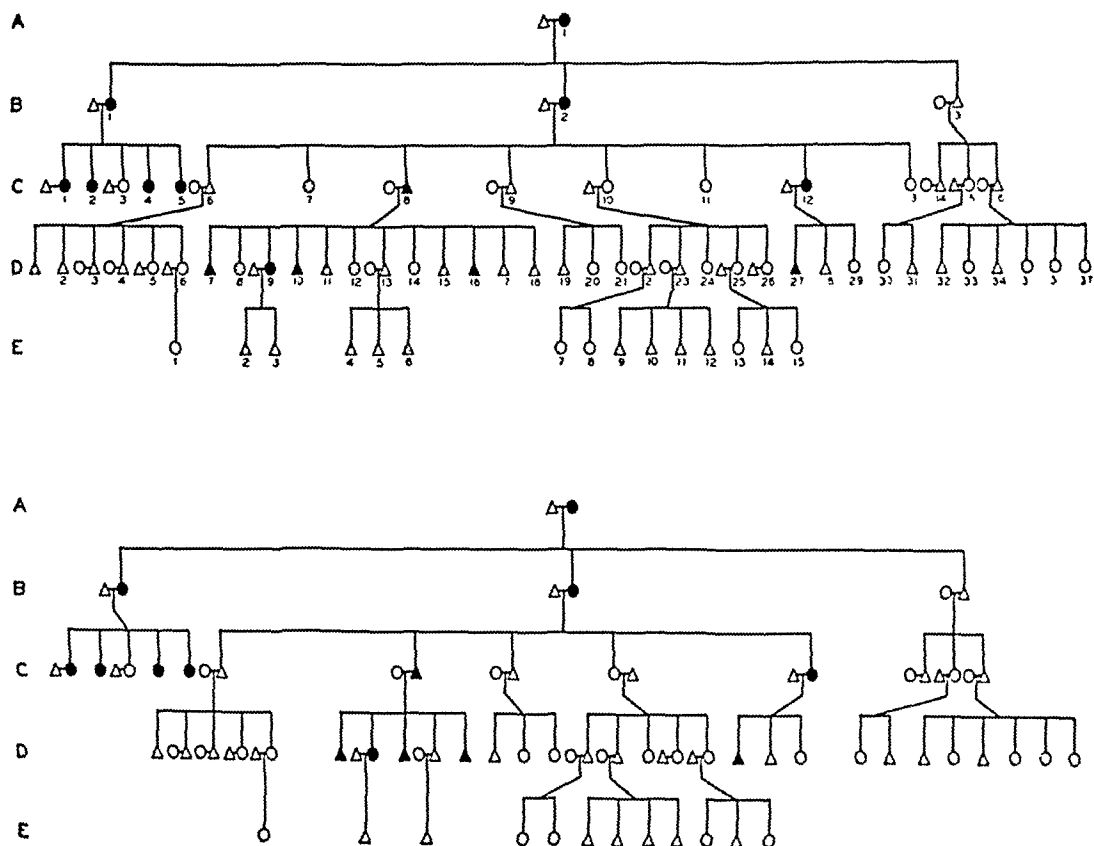


CHART I—Showing, graphically, the descendants of Mrs X, who had multiple skin tumors and a “lump as large as a bucket hanging from her neck”

Mrs X, who is the only known member of the oldest generation, is represented as A1. The affected individuals are shown in solid black circles (females) or triangles (males). The stippled figures represent those children who died in infancy, and it is uncertain whether or not they would have shown stigmata of von Recklinghausen's disease. The members of the youngest, or E, generation are too young as yet to be sure they are all unaffected.

The lower chart represents the same family tree omitting those children dying early in life, better to show the mendelian inheritance of the disease.

be due to its existence in the members of that apparently unaffected generation in a mild form, the so-called *forme frustée* which is characterized only by a number of *café au lait* spots.

The Pathologic Aspects of Multiple Neurofibromatosis—Although the association of the multiple encapsulated subcutaneous tumors with the nerve trunks was recognized in 1849¹¹ (33 years before von Recklinghausen's description of the condition), there have been numerous divergent interpretations of the morphology of the disease since that date.*

* It is of interest to record here that a similar condition has been described in animals by veterinarians.¹²

Neurofibromata may be found on the branches of the cutaneous nerves along the trunks of the nerves of the thorax and extremities and arising from the cords and trunks of the brachial and lumbar plexus. They may also arise from the paravertebral sympathetic chain, the visceral sympathetic plexus or the nerve supply of the intestinal tract and enlargement of the periarterial sympathetics suggesting such a tumor formation has been recorded¹³. Also tumors are at times found on the cranial nerves within and without the cranial cavity and along the spinal nerves before they emerge from the spinal canal. Growths arising from the meninges¹⁴, intracerebral astrocytomata and ependymomata and syringomyelitic changes¹⁵ in the spinal cord have been reported in certain cases of von Recklinghausen's disease.

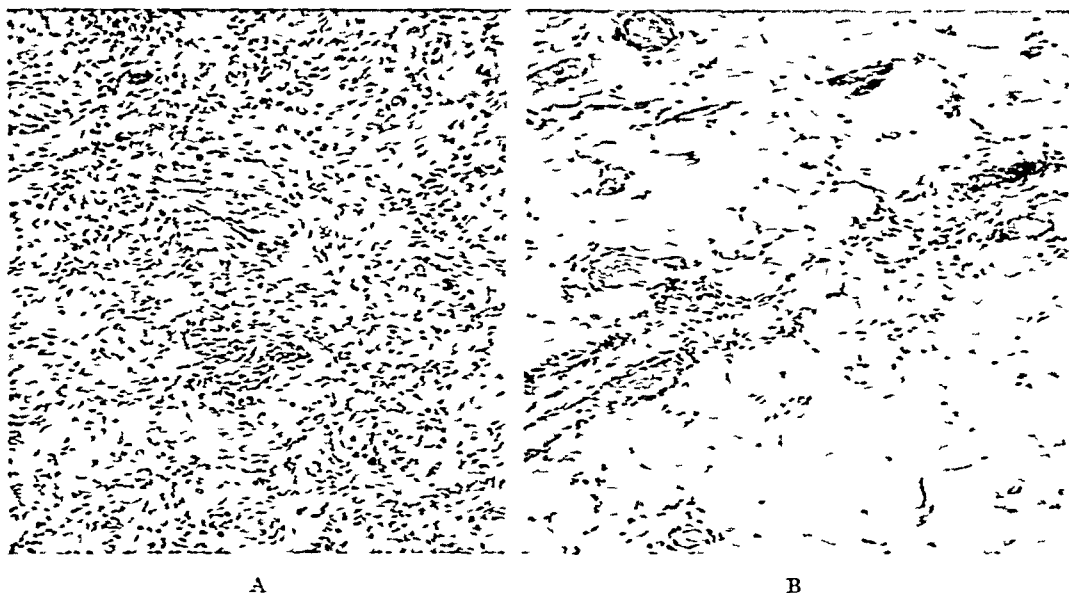


FIG. 1—(A) The disorderly cellular arrangement seen in the microscopic section of the tumors of von Recklinghausen's disease (Fig. 12) is well represented by the area shown above. In certain tumors the fibroblastic element predominates to such a degree that the palisading of the nuclei and regularity of the cells suggests the picture seen in a neurinoma. Other nodules from the same patient having a predominance of loose areolar stroma may show the appearance of the tissue removed from the pachydermatocele (B).

(B) Section of the jelly-like material from the patient shown in Figures 15, 16 and 17 with its thin walled large blood vessels and acellular structure contrasts sharply with the fibroblastic reaction in other lesions of the same disease process. The variations in, or predominance of one of these contrasting types of tissue accounts for the wide differences in the physical characteristics of the individual tumors.

At the present time among those¹⁶ who have investigated the structure and origin of the multiple neurofibromata there is some difference of opinion concerning the exact interpretation of their observations. Verocay and Masson^{17a} believe that the tumors are neuroectodermal in origin arising from the sheath of Schwann and Cushing¹⁷ has recently called attention to early experimental work showing that neuroectoderm, although peculiar in its origin, should be considered a sheet of cells such as the mesoderm which possesses the ability under certain circumstances to give rise to a variety of tissues. None the less Penfield's¹⁸ belief that the multiple neurofibromata of von Recklinghausen's disease are of mesodermal origin arising from the epineurium, perineurium and endoneurium of the nerve bundles has gained wide attention at present.

The latter author describes a characteristic section of one of these nerve tumors as showing "tangled reticular areas where the nuclei are not arranged in any particular order (Fig 1 A) and where there is an obvious confusion of connective tissue. Nerve fibers may be demonstrated in the capsule and passing through the tumor itself and collagen stains of the reticular areas show a crossing and intermixture of fine collagen fibers. In areas of degeneration or softening, much hyaline material may be present, and while the nerve fibers passing through the tumor are usually nonmyelinated, myelinated fibers may be present. Areas of perineural fibroblastic reaction may be so extensive as to almost replace the more reticulated tissue."

The skin pigmentation, which is seen on all affected individuals, may be



FIG 2—(A) A symmetrical, triangular pigmented area having all the characteristics of a large *café au lait* spot may be seen covering the lower abdomen, inguinal regions, and extending down onto the genitalia of a 23 year old student. More characteristic, is the elliptical *café au lait* spot visible on the right side of the abdominal wall lateral to and just above the umbilicus. The small pigmented dots are freckles. Also, a number of small subcutaneous tumors may be seen. (B) On the lower back and thighs are medium sized *café au lait* spots. The scoliosis occurring so frequently in individuals affected with von Recklinghausen's disease may be seen in the posterior view.

represented by a moderate freckling in mild cases, while in others it may be diffuse and frequently has a symmetrical distribution (Fig 2). True nevi, although not characteristically associated with the disease, are at times seen and may reach the size of the so-called "bathing trunk nevi."¹⁹ The texture of the skin of a *café au lait* spot may be coarser than normal but usually there is no appreciable gross change aside from the increased pigmentation.

It is stated that microscopic sections of the *café au lait* spots may show an increase in the pigment of the basal layer of the epithelium.²⁰ This has not been noted in the group of cases seen by us, but these have shown an increase in the number of melanophores in the deeper layers of the dermis, especially about the small blood vessels, a change which may well account for the pigmentation.

The skeletal changes associated with multiple neurofibromatosis have been well described by Brooks and Lehman.²¹ Scoliosis (Fig 3) and irregularity

in the shafts and differences in the length of the long bones have been the abnormalities most frequently noted. Pseudarthroses and abnormal curvatures of the bones have also been reported²⁰. The bone changes have been interpreted by Brooks and Lehman as due to the involvement of the bone by the growth of tumor tissue characteristic of von Recklinghausen's disease. They state that the growth of a neurofibroma of a periosteal nerve may be accompanied by a certain amount of bone destruction and bone regeneration. If in the process of development the osteogenetic element of the periosteum covers the tumor, a thin shell of bone may be formed, giving the appearance of a subperiosteal bone cyst. If the growth destroys the epiphyseal cartilage, shortening may follow, while with the lesion limited to the shaft, lengthening

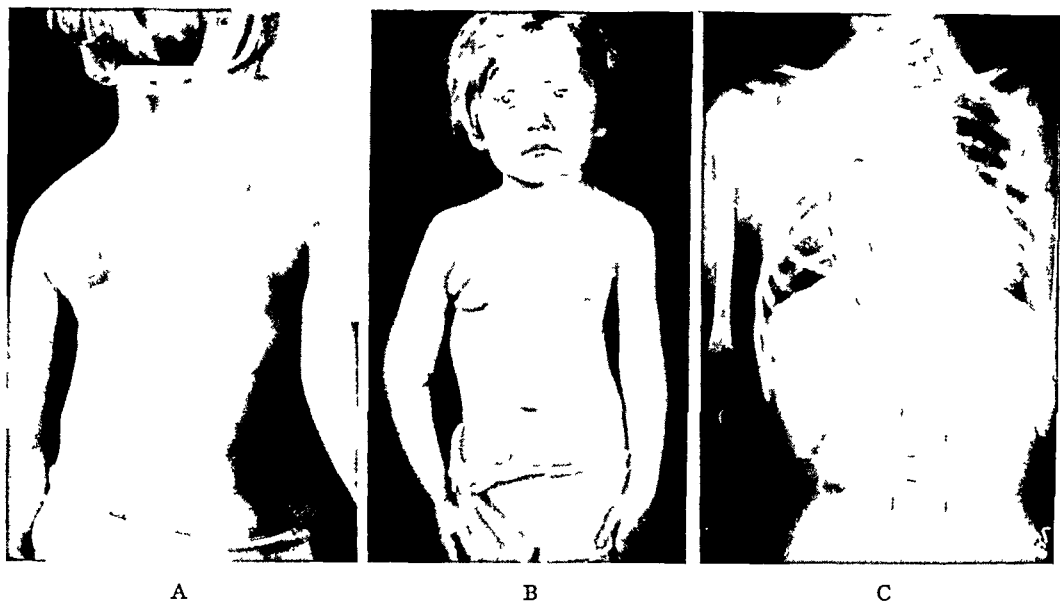


FIG 3—Hosp No 38744 D. H., female, white, age four, had several areas of skin pigmentation present at birth, and the spot above the right scapula has grown progressively larger since. The curvature of the spine was first noted by the parents when she was three years of age, and this too had increased during the year preceding admission to the hospital. On entry into the hospital she showed multiple neurofibromatosis with numerous subcutaneous nodules and *cafe au lait* spots (A and B). The scoliosis so frequently encountered in patients having von Recklinghausen's disease is shown in a marked degree (A, B and C).

may occur. Scoliosis may follow abnormal softening of the vertebrae as a result of the tumor growth, or it may be secondary to growth disturbances in the lower extremities.

In general, neurofibromata are benign encapsulated tumors, although at times their capsules may be poorly defined. They do not, as a rule, destroy the nerves from which they grow. Malignant tumors occur in from 12 to 14 per cent of patients showing stigmata of von Recklinghausen's disease. These are usually fibrosarcomata, but epithelial neoplasms, thought to arise from the sheath of Schwann, have been reported²². All grades of malignancy may be encountered in a large series of these lesions, and, although local invasion is the usual method of extension, metastases to distant organs, particularly the lungs, may occur. Rarely, metastases may occur to adjacent lymph nodes.

(Fig 14) Not infrequently, more than one malignant tumor may arise at different levels along the same nerve trunk

The Clinical Features of Multiple Neurofibromatosis—It has well been said that multiple neurofibromatosis is a disease of protean manifestations,²³ for the individual variations in the classic clinical pictures alone are without limit. Although the stigmata of the process, either subcutaneous tumors or areas of skin pigmentation, have not infrequently been observed in infants, the presence of the disease has been more often recognized at puberty as it is more usual at this period for the subcutaneous nodules to make their first ap-



FIG 4—Two patients illustrating the difference in appearance of fibroma molluscum (A and B) and plexiform neuroma (C). (A) Fibroma Molluscum. This pendulous tumor composed of fibrous tissue (B) overlay the back and dorsal vertebrae of a colored man, age 25, who was hospitalized because of a paraplegia of two weeks' duration. At operation, the spinal cord was found to be pulled completely apart by traction over the gibbous. There was no evidence that pressure had been made on the cord at the point of division.

(B) A gross section of the fibroma molluscum shown in (A) reveals an unusual amount of pigmentation. On microscopic examination this tumor was composed of uniform fibrous like tissue with large collections of melanin scattered throughout the deeper portion of the growth.

(C) The growth present over the left hip of another patient is irregular rather than uniform in consistency and on palpation gives the impression of being composed of interlacing nodular cords and is more likely a plexiform neuroma. This 39 year old colored woman first noticed a "fleshy lump" here when she was age 12, and the tumor has increased progressively in size since then. There is also a hard, tender, painful mass on the medial aspect of the left upper thigh which has grown rapidly during the past three months and is clinically a sarcoma.

pearance or to reach such a size that they are noticed by the patient or his family.

The usual clinical picture is that of multiple sessile or pedunculated soft or elastic tumors (which may number as many as 4,500)⁴ associated with *café au lait* spots (Fig 3), both the tumors and pigmented areas showing infinite variations as to size, number, consistency and location. In addition to the characteristic well-defined, more or less globular subcutaneous nodules over which at times the skin may be atrophic, one may encounter the soft pendulous masses of fibroma molluscum (Fig 4 A and B), or the worm-like plexiform

neuromata (Fig 4 C), which have acquired special designation as clinical and pathologic variants of the lesions usually seen in von Recklinghausen's disease. Elephantiasis neuromatosa, an enlargement of an extremity resembling that seen in elephantiasis (Fig 5), is an infrequent variant of the classic clinical picture, and is associated with tumor formation or diffuse enlargement of many of the nerves of the limb, at times even the sympathetics being involved.¹³

The *café au lait* spots, varying in size from freckles to pigmented areas 10 cm or more in diameter, are found in all cases, and although they are usually ellipsoid in shape they may be irregular in outline. They are often symmetrically distributed over the trunk and extremities (Fig 3). Nevus anemicus has been described²⁴ in association with the disease, and while nevi

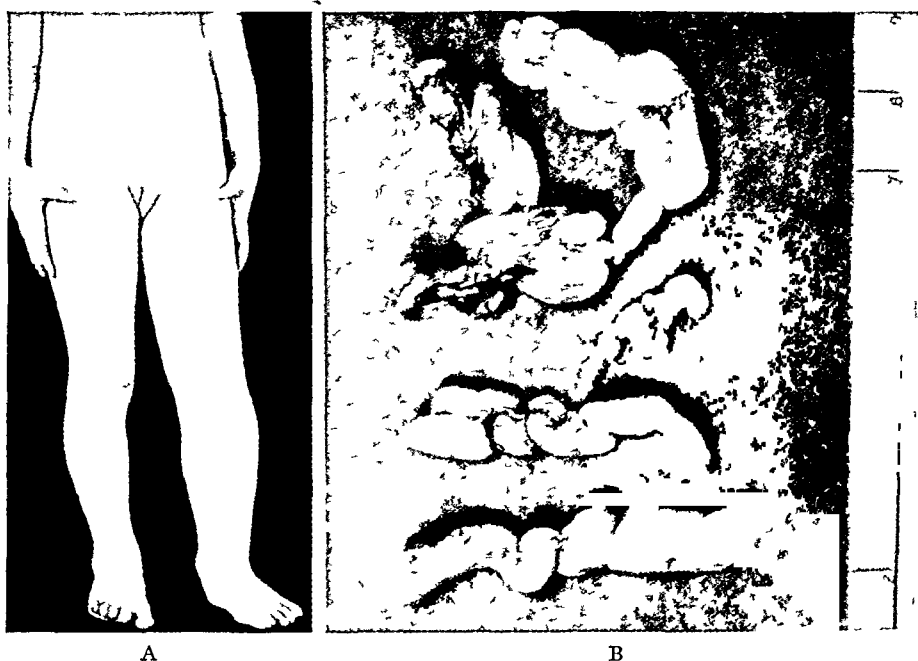


FIG 5—Elephantiasis Nervorum (Lewis, Dean and Hart, Deryl Tumors of Peripheral Nerves. ANNALS OF SURGERY, 92 961-983, 1930)

The left lower extremity is enlarged. Multiple nodules can be palpated along the nerves, especially over the short saphenous. A biopsy was performed and the nerves were found to be irregularly enlarged throughout their entire exposed length, varying in size from one to several millimeters in diameter.

and angiomata are not infrequently present these do not bear the same intimate relationship to the multiple neurofibromata as do the *café au lait* spots, and should not be confused with the latter.

Sharpe and Young^{3b} have emphasized recently, that one of the most outstanding features of von Recklinghausen's disease is its progressive course. As the individual matures the tumors increase in number and size, and the skin pigmentation becomes more widely distributed. This course of events was brought forcibly to our attention by one of our patients who stated that as a boy he had few tumors, but, that with the advancing years, not only did the original tumors enlarge, but new ones appeared so that his trunk became studded with them (Fig 6). One of his sons, as a child, had only a few *café au lait* spots, noticed the appearance of subcutaneous tumors at puberty, and, as he has grown older, both types of lesions have increased in size and number.

Unrelated or intercurrent pathologic disturbances and even normal physiologic changes may exert a definite influence on the evolution of the disease process. It is well known that puberty has a stimulating effect on the development of the lesions and pregnancy as a rule is attended by an increase in the size and number of tumors and *café au lait* spots. We have observed an increase in the intensity of the skin pigmentation of one of our patients during pregnancy. Recession of both types of lesions following delivery, and exacerbations during subsequent pregnancies have been reported.^{25a,b,c} Intercurrent

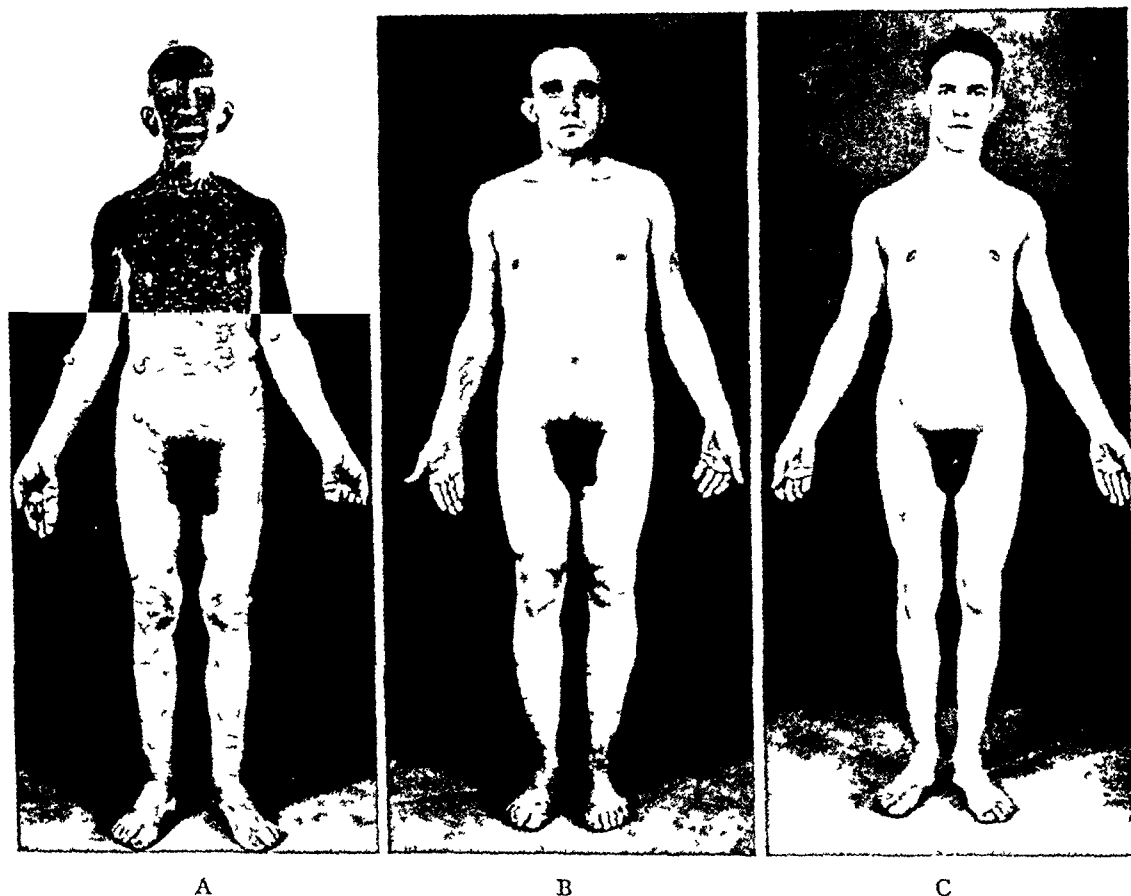


FIG 6—(A) E. P., who is at present 62 years of age, is represented by the triangle C 8 in Figure 1. As a young man he had few subcutaneous tumors, but these became larger and many others appeared as he grew older.

(B) R. N. P., his oldest living son (D 10 Fig 1), as a child, had a few *café au lait* spots, but developed subcutaneous tumors at puberty, and as he has grown older both types of lesions have increased in size and number. A tumor removed from the abdominal wall showed the microscopic appearance of a neurofibroma of von Recklinghausen's disease.

(C) J. R. P., another son of E. P. (D 13 Fig 1), has no demonstrable neurofibromatosis or *café au lait* spots.

infections may also cause an increase in the symptoms and signs of the condition and these may recede following recovery.

A high incidence of feeble-mindedness has been recorded in those showing marked involvement⁴ and we have noted a certain lack of mental acuity in the more markedly affected members of the family reported by us (Chart 1). The lack of fertility in some families showing extensive neurofibromatosis has been ascribed to sexual impotence and the dying out of other strains has resulted from a high infant mortality (Chart 1). Obvious endocrine dysfunction has been observed in many instances.²³⁻²⁶ The pigmentation in certain patients

has been explained by disordered adrenal function, and acromegalic features in others have been related to pituitary dysfunction. However, there is little evidence pointing toward a constant disturbance of function of any of the endocrine glands as the underlying cause of multiple neurofibromatosis and manifestations of such dysfunction in a particular individual may be attributed to pressure effects of neurofibromata on the gland in question, or to some coexistent developmental disturbance.

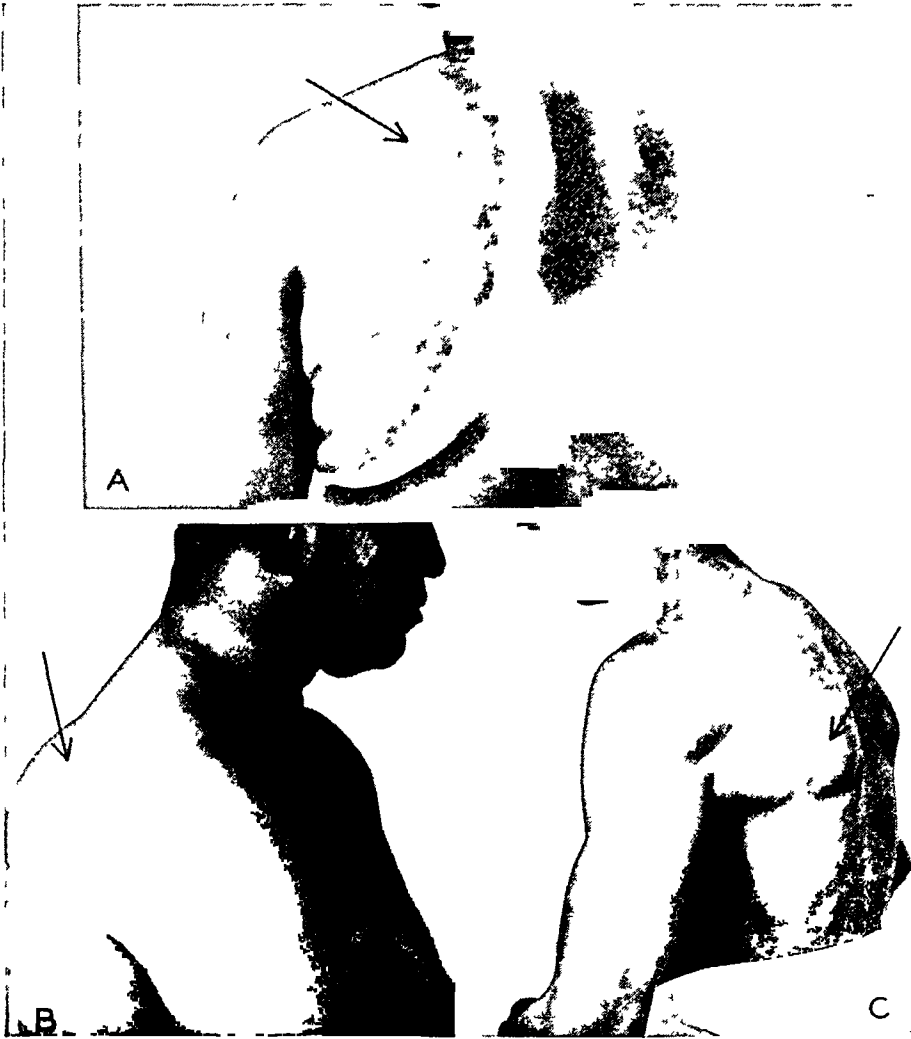


FIG 7—Lipomata in the subcutaneous tissue overlying the scapulae of a mother and two sons. These are the only lipomata present in these patients. Two of the patients show sebaceous cysts which might increase the possibility of confusing this condition with neurofibromatosis.

Although the clinical and pathologic variations discussed above go far toward making multiple neurofibromatosis a disease of protean manifestations, none the less, it is frequently the complexity of the symptoms and signs resulting from one of the complications of the malady which presents a major problem in clinical interpretation. Both the bizarre forms of the disease and the complications present problems in differential diagnosis.

Differential Diagnosis—It has been necessary, in our experience, to dif-

ferentiate multiple lipomata (Figs 7 and 8), multiple xanthomata, multiple epidermoid cysts (to be published), lymphosarcoma and Hodgkins' disease from multiple neurofibromata. Leprosy, especially in subtropical countries, must also be considered in patients with numerous subcutaneous tumors. Although the absence of *café au lait* spots is usually sufficient to eliminate von Recklinghausen's disease as a probability in a patient showing symptoms and signs suggestive of one of the diseases noted above, the clinical differentiation is made difficult in many individuals by the presence of a certain amount of normal freckling. Scoliosis associated with multiple subcutaneous nodules is also of value as a diagnostic sign, although scoliosis due to other causes is

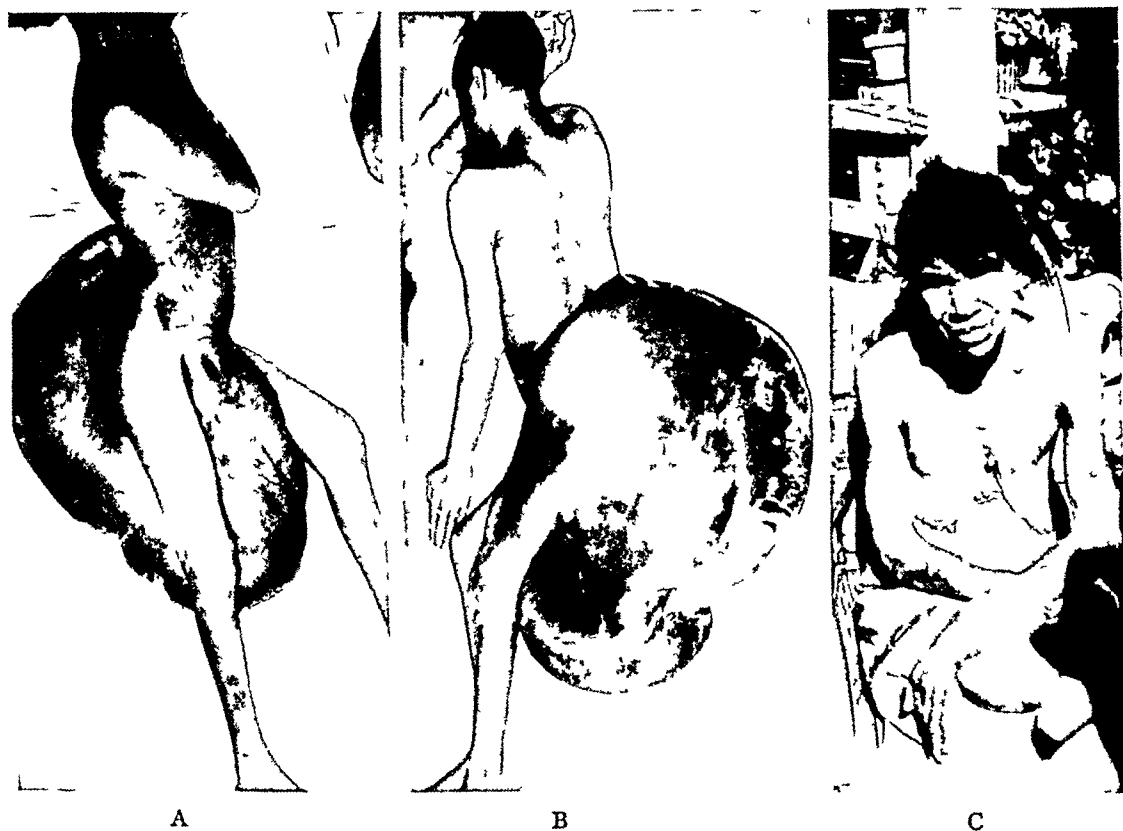


FIG 8—The colored man, age 36, shown above (A and B), first noticed a small mass on his right buttock as a child and the tumor had grown progressively larger until the time of his entry into the hospital. Although he had been able to walk about the greater part of his life he had been completely bedridden during the two years prior to admission. The growth was thought to be a fibrolipoma until the skin pigmentation and multiple subcutaneous nodules on the extremities and trunk were discovered. Microscopic examination of one of the small tumors, which was removed, showed the characteristic appearance of a neurofibroma of von Recklinghausen's disease. Microscopic sections of tissue taken from the large growth showed very compact fibrous tissue but nothing suggestive of a malignant tumor. However, this would not rule out a malignant change in other parts of the growth. The patient's family history could not be followed for more than two generations. His mother, shown above (C), had multiple neurofibromatosis.

common and its presence together with subcutaneous tumors cannot be relied upon as an absolute criterion for the diagnosis of multiple neurofibromatosis. In the usual case, the character and distribution of the subcutaneous tumors and *café au lait* spots make the clinical diagnosis an easy one. When there is any doubt as to the diagnosis, pathologic study of the lesion in question is indicated, especially should the clinical features of one or several of the tumors raise the question of malignancy.

The Surgical Problems Presented by Multiple Neurofibromatosis—The

patients who develop surgical complications as a result of von Recklinghausen's disease may be classified in three main groups. The largest group consists of individuals having neurofibromata in such a location that pressure from the tumor growth affects the function of one or more important organs or structures. In the second group are the patients who develop a malignant growth in the course of the disease, and the third is made up of those patients

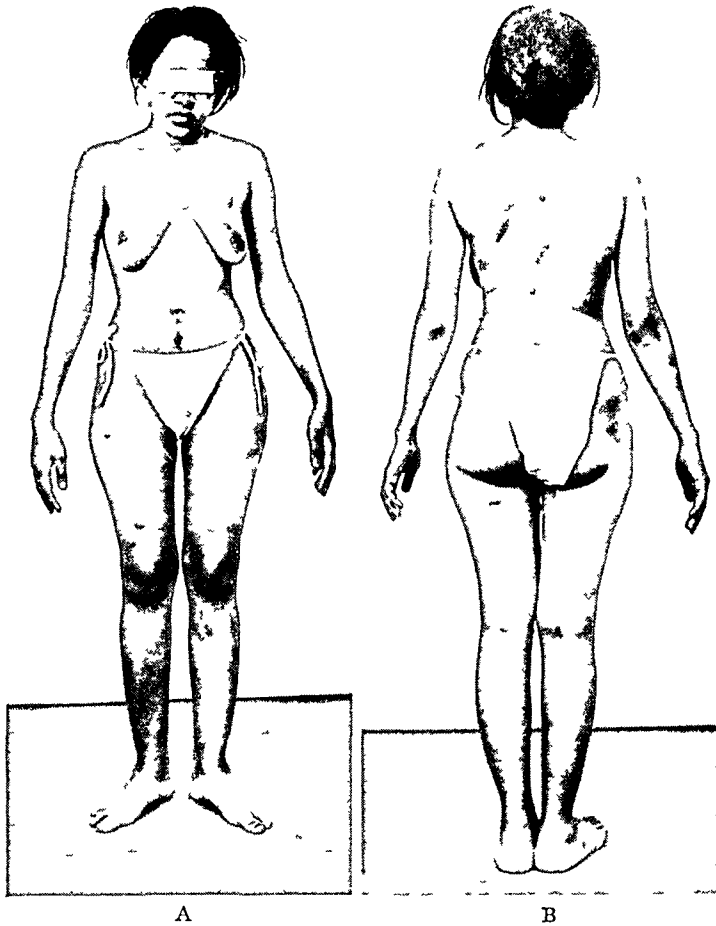


FIG. 9.—This 26-year-old woman was admitted to the Tumor Clinic of the Duke Hospital complaining of a painful tender tumor in the left breast above the nipple. She had noticed the presence of painless subcutaneous tumors since early childhood, all of which increased slowly in size as she grew older. The growth of which she complained had been present for five years but had been painless until three months before her visit to the hospital when it became tender and caused a drawing pain in the adjacent area. Following excision of the pigmented, conical mass, which on removal was found to be somewhat nodular she has been entirely free of pain for over a year. Microscopic study of the tissue showed a neurofibroma such as is encountered in von Recklinghausen's disease with nothing to suggest a malignant growth. Note also the scoliosis.

having a hemorrhage into a large pachydermatocele, which is occasionally seen in neurofibromatosis.

The pain caused by the growth of a tumor on a peripheral nerve has previously been reported,²⁷ and a case recently seen by us illustrates this pressure effect (Fig. 9). The bizarre symptoms and signs resulting from intracranial tumors associated with generalized neurofibromatosis, have been

commented upon by Cushing¹⁷ and others^{5, 14}. Cranial nerve palsies and clinical signs of pressure of the tumors on the brain stem are not uncommon. Tumors arising from the nerve roots within the spinal canal are occasionally seen and may result in signs of cord compression (Fig 10). Partial obstruction of the pharynx from neurofibromata,²⁸ macroglossia from similar lesions in the tongue²⁹ and tumors in the neck arising from the cervical nerves and brachial plexus may occur (Fig 16). We have studied one patient, an individual with numerous masses in the neck and an incomplete tracheal obstruction produced by mediastinal neurofibromata, whom we wish to report in



FIG 10—(A) This patient, a white boy, 16 years of age, was admitted to the Neurosurgical Service of the Duke Hospital for treatment of a paraplegia of six years' duration. Since birth, he had had a boggy, subcutaneous tumor over the right scapula and, during the past year, other subcutaneous tumors and *cafe au lait* spots had appeared. The paralysis developed gradually over a period of "several months" and the loss of motor function was followed shortly by anesthesia over his lower extremities and trunk up to the level of the nipples. A laminectomy revealed an intraspinal neurofibroma (B) originating from the eighth cervical nerve root extending from the sixth cervical to the second thoracic vertebrae completely filling the spinal canal extending out into the foramina and, undoubtedly, connected to the tumor in the chest (C) which had reduced the cord to a thin filament. On an adjacent nerve root there were two small neurofibromata which were also removed with the nerve root.

(C) Roentgenograms of the chest taken before operation showed a tumor in the upper left chest and lower neck, and a diagnosis of an hour glass tumor was made. The intrathoracic tumor has not been removed since it is producing no symptoms and it seems unlikely that there will be any return of function in the cord.

detail, since she illustrates so well one of the surgical problems resulting from pressure symptoms.

Case Report—Hist No A-6790 V E R (Fig 11), white, female, age 19, was referred for treatment because of a mass in the upper mediastinum which was partially compressing the trachea and the upper lobe of the right lung. There was no history of skin pigmentation or of subcutaneous tumors occurring in other members of the family. At age 9, she had an attack of Rocky Mountain spotted fever and following this a small mass was noted in the subcutaneous tissue over the left shoulder. Four years before admission, at age 15, she developed intermittent attacks of dull aching pain in the region of the right shoulder, right clavicle and right side of the chest, which had persisted. The

episodes of pain came on at intervals of several months and were of three to four days' duration. For three weeks before she entered the hospital, she had experienced some difficulty in breathing. Nodular masses were noted on both sides of her neck two weeks before entry and had increased gradually in size.

Physical Examination revealed several *cafe au lait* spots on her trunk and numerous small, soft and elastic tumors in the subcutaneous tissues over her back and extremities. On the right side of the neck, anterior to and beneath the sternocleidomastoid muscle, were several firm, slightly tender masses which resembled a chain of enlarged cervical

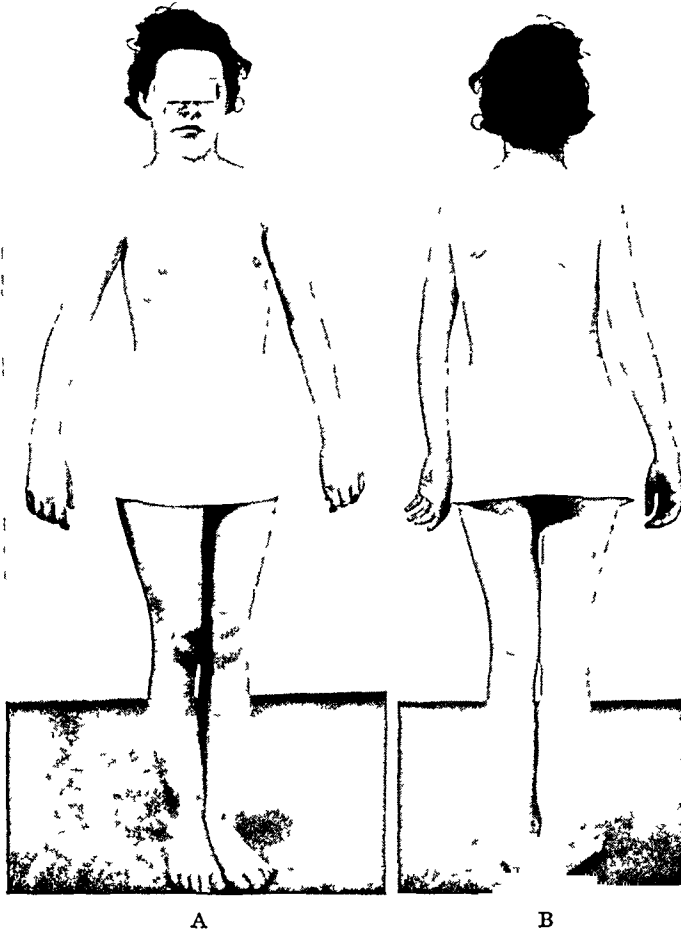


FIG 11—This white girl, age 19, was referred to the Duke Hospital for treatment of a growth in the upper mediastinum partially compressing the trachea and the upper lobe of the right lung and causing pain in the right chest and shoulder. When first seen in another hospital, the clinical impression was either Hodgkin's disease or lymphosarcoma since she had numerous masses in the neck and both axillae, resembling enlarged lymph nodes. A biopsy of one of the tumors showed the characteristic picture of a neurofibroma of von Recklinghausen's disease and further examination revealed numerous subcutaneous tumors and *cafe au lait* spots. The scar from the thoracotomy can be seen located medially and inferiorly to the scapula. The moderate scoliosis is not seen clearly in (B).

lymph nodes. Several tumors in the axillae felt much like enlarged lymph nodes but two removed for study before admission had proved to be neurofibromata. There was a scoliosis of the dorsal spine with the convexity to the left.

The laboratory studies of the blood and urine revealed normal findings and the blood Wassermann was negative. A roentgenogram of the chest (Fig 12 A) showed a rounded mass present in the upper mediastinum which extended outward to compress the upper lobe of the right lung.

Our impression was in agreement with the previously made diagnosis of von Recklinghausen's disease with intrathoracic and probably mediastinal neurofibromata. In view of the patient's respiratory symptoms it was thought advisable to attempt removal of the intrathoracic tumors.

Operation—August 30, 1938, Dr Deryl Hart. Under nitrous oxide and oxygen anesthesia, a posterior thoracotomy was performed on the right side. The incision exposed, in the subcutaneous tissue and muscle, a large number of small, elongated neurofibromata. Three firm tumors (Fig 12 C) located in the costovertebral sulcus, one of which extended into the mediastinum partially compressing the trachea, were exposed and removed, relieving the patient of all respiratory difficulty. Pathologic examination of the tumors showed them to be neurofibromata, similar in appearance to those encountered in von Recklinghausen's disease (Fig 1 A). A roentgenogram of the chest

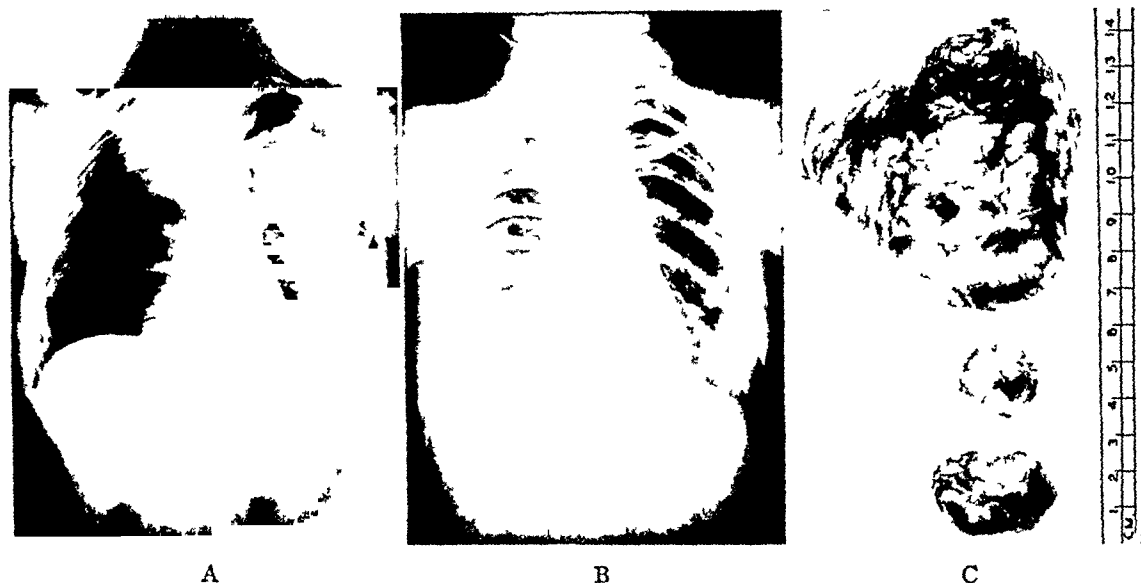


FIG 12—Roentgenograms of the chest of the 19 year old girl shown in Figure 11 taken before (A) and after (B), a posterior thoracotomy with removal of the intrathoracic neurofibromata. The rounded mass in the upper chest, extending into the mediastinum and partially compressing the trachea and the upper lobe of the right lung, seen in (A), was found at operation to be composed of three tumors (C) (for microscopic appearance see Figure 1A) which apparently arose from the paravertebral sympathetic chain, although the possibility of their origin from the intercostal nerves at the vertebral foramina (hour glass tumors of Heuer and others) could not be completely excluded. Following their removal the upper lobe of the right lung re-expanded (B) and all pain and symptoms of tracheal obstruction disappeared. Since operation the right hand has remained persistently warmer than the left, probably as a result of damage to the sympathetic nerve supply.

subsequent to operation showed re-expansion of the right upper lobe and some general fibrosis of the right lung (Fig 12 B).

It seems most likely that these tumors originated from the thoracic sympathetic trunk since they were most firmly attached in this region and the right hand and arm have been warmer than the left since operation. They may have originated from the thoracic nerves at their point of emergence from the spinal canal but there was no evidence of any intraspinal extension as in the hour-glass type of tumor described by Heuer, Andrus and Taylor³⁰. Hypesthesia has been present over the right chest since operation but this is limited to the area innervated by the nerves that were divided in making the thoracotomy incision.

The case reported above also showed the dorsal scoliosis (Fig 10) so frequently encountered in this disease, in this instance probably the result of the intrathoracic tumors. The change in the spinal column may be marked and,

instead of scoliosis, a gibbous may develop and may be followed eventually by a paraplegia. This course of events, previously reported,³¹ was seen in a patient recently studied in the Duke Hospital, in whom a laminectomy disclosed the spinal cord to be completely torn across by traction over the kyphos (Fig 13)

Tumors of the abdominal viscera have been noted frequently but apparently very rarely give rise to pressure symptoms. An exception to this was the case of a patient³² with an abdominal neurofibroma, causing marked abdominal distension and dyspnea, which was thought to have arisen from the sympathetic nerves of the ovary. Tumors of the retroperitoneal nerves are more common



FIG 13—This colored man, age 25, was found at operation to have the spinal cord completely divided by traction over the extremely pronounced kyphos. (See Fig 4 A and B, same patient). He suddenly developed a paraplegia two weeks before admission to the hospital. In addition to the pendulous fibroma molluscum below the gibbous, he also showed numerous neurofibromata in the subcutaneous tissues of the trunk and extremities.

and have been reported as a cause of dystocia during pregnancy,^{25c} while neurofibromatosis of the prostate and bladder may be a cause of serious urethral and ureteral obstruction which may result in uremia.³³

Large benign neurofibromata may cause some discomfort from their size. However, a rapidly growing tumor should make one suspicious of malignancy. The incidence of sarcomatous degeneration in von Recklinghausen's disease has been found to vary from 12 to 13 per cent.^{31a, b, c} Stewart and Copeland,³⁵ reporting 21 cases of neurogenic sarcoma developing in patients with multiple neurofibromatosis, found two peaks in the curve of age incidence—one between the ages of one and ten years and the other between 30 and 50 years. Metastases have been noted in 22 per cent of such cases.^{34c} Once malignancy develops, the prognosis is poor, and of the group of patients reported by Stewart and Copeland³⁵ none was well at the end of five years. Local recurrence, which usually follows excision of one or more malignant tumors

arising from the same nerve sheath, often necessitates secondary operations. The majority of the patients finally die as a result of local recurrences or metastases. Metastasis to regional lymph nodes, an infrequent occurrence, is illustrated by one of our recent cases (Fig 14). Radical surgical excision or amputation has been the usual treatment of these sarcomata and remains the accepted procedure. Stewart and Copeland³⁵ state that certain tumors of long duration have recurred after operation and the patient has been made worse by excision. They also suggest that a policy of nonintervention may be the treatment of choice for slow-growing malignant tumors of this type. Irradiation therapy of these sarcomata has not been standardized and while it may be beneficial in some cases no conclusions can be drawn as to its effectiveness in general.



FIG 14—Metastases in the inguinal lymph nodes, 15 months after amputation for a spindle cell sarcoma arising in the upper end of the right tibia in a patient with von Recklinghausen's disease. This patient, a white man, age 35, had multiple neurofibromata with characteristic *café au lait* spots. Sections of the growth in the tibia showed a cellular structure similar to other sarcomata developing in our group of patients with von Recklinghausen's disease. A roentgenogram of the chest, taken before amputation, showed, on the left, a tumor, projecting above the diaphragm, near the heart, and thought to be a neurofibroma and not a metastasis. Since amputation, this has increased somewhat in size, is not located within the lung, and is not considered to be a metastasis.

The second case we wish to report in detail, presents an excellent example of the third type of surgical complication seen in von Recklinghausen's disease. This patient eventually died of asphyxia caused by a rapidly growing and clinically malignant tumor in the neck, but entered the hospital on account of symptoms resulting from a spontaneous hemorrhage into a pachydermatocele over the lumbar region.

Case Report—Hist No 69788 M E S (Figs 15, 16 and 17), white, female, married, age 23, was admitted to the Duke Hospital, July 12, 1936, complaining of a swelling over the lower back of nine days' duration. Her mother and one sister had skin tumors over the trunk and extremities similar in character to those present on the patient. As a child she had a club foot on the right side which had been partially corrected by operations when she was 17 and 19 years of age. Not until she was 13 years of age were the subcutaneous nodules noted over the trunk, and at the age of 17, a mass in the left side of the lower neck first appeared (Fig 16). This increased very gradually in size until the year before admission, when its growth became accelerated.

The illness for which she sought hospital care developed nine days before entry, when a "lump of muscle," which she had "always had" over the lumbar region, enlarged rapidly during a period of 48 hours. At this time, she became very weak and fainted when she attempted to get out of bed. There was no history of any injury, and aside from the aching discomfort in the region of the tumor she was free from pain. The family physician aspirated blood from the swelling and regarded the condition as a subcutaneous

hemorrhage Cold packs were applied to this area which became somewhat softer, but since it did not decrease in size she was eventually sent to the hospital, nine days after the onset of her acute symptoms



FIG 15—Same patient as shown in Figures 16 and 17 This patient, white, female age 23, was admitted to the Duke Hospital nine days after a spontaneous hemorrhage into the pachydermatocele over the lumbar region From a small inconspicuous "lump of muscle" the tumor grew to the size of a "football" within a few hours The subcutaneous nodules and *cafe au lait* spots over the trunk and extremities have been present since adolescence On the side of the ankle can be seen the scar resulting from operations for a congenital club foot



FIG 16—Same patient as shown in Figures 15 and 17 The rapidly growing tumor present on the left side of this patient's neck was clinically malignant and eventually caused her death from asphyxia At the time of operation for a hemorrhage into the pachydermatocele respiratory embarrassment due to this growth necessitated intratracheal anesthesia She would allow no treatment for this mass and it caused her death by asphyxia five months later

Physical Examination showed a pale, well nourished patient, with normal temperature, pulse and respiration The skin was studded with multiple, soft, elastic tumors, characteristic of those seen in von Recklinghausen's disease, and there were numerous

cafe au lait spots scattered over the trunk. A certain amount of mental retardation was obvious. On the left side of the neck, beneath the carotid, and extending down behind the clavicle and sternum, displacing the trachea to the right, was a firm, fixed tumor, approximately 12 cm in diameter (Fig 16). Examination of the heart, lungs and abdomen was essentially negative. Overlying the lower lumbar region was a mass about the size of a football, over which the skin was tense, shiny, and discolored by the underlying hematoma. The swelling was warm, pseudofluctuant and nontender (Fig 17). The right leg was larger than the left and the right foot, in addition to being fixed in dorsiflexion at the ankle, showed, on the anterolateral aspect, scars of the previous operations.



FIG 17—Same patient as shown in Figures 15 and 16. The blue discoloration of the skin overlying the hemorrhage in the pachydermatocele resulted in the diagnosis of subcutaneous hemorrhage by the patient's family physician. At operation more than a liter of partially clotted blood was evacuated from the hematoma in the gelatinous tumor tissue, and the greater portion of the tumor was excised (see Figure 1 B for microscopic appearance). The patient made a satisfactory convalescence and she had no further bleeding during the remaining five months of her life (Fig 16).

Studies of the blood revealed Hb 44.2 per cent, RBC, 3,700,000, WBC 9,400. The urine and blood Wassermann examinations were negative. The blood cholesterol was 183 mg per cent. Roentgenograms of the lumbar spine showed an enormous soft tissue tumor in this region and an erosion of the spinous processes of the upper three lumbar vertebrae.

A diagnosis of hemorrhage into a pachydermatocele over the lumbar region was made and after transfusions (totaling 1,500 cc), which resulted in raising her hemoglobin to 81 per cent, the hematoma was evacuated under nitrous oxide and oxygen anesthesia. Since respiration was considerably embarrassed by the cervical tumor it was necessary to use intratracheal anesthesia. The liquefied blood and blood clot were removed from the surrounding gelatinous tissue which represented the preexisting tumor. There was a little oozing from smaller vessels in the walls of the resulting cavity after evacuation of the hematoma but no large bleeding point could be seen. The gelatinous tumor tissue was removed as widely as possible, exposing the lumbar fascia in the depth of the wound. After closure of the skin a pressure dressing was applied to obliterate the dead space. Six weeks later there was only a small swelling in the lumbar region occupying the site of the former pachydermatocele.

She refused treatment for the rapidly growing cervical tumor and her family physician wrote, five months later, that she had died rather suddenly of asphyxia as a result of this

growth which had continued to increase in size after her return home. There was no recurrence of hemorrhage into the tumor over her lumbar region.

We have been able to collect from the literature seven other cases of hemorrhage into large tumors observed in patients having multiple neurofibromata, which are briefly summarized below.

ABBREVIATED CASE REPORTS OF SEVEN INSTANCES OF HEMORRHAGE INTO NEUROFIBROMATA

(From the Literature)

Case 1—Reported by Heuer,¹⁹ 1917

A 24 year old machinist was first operated upon in 1906 for hemorrhage into a large nevus over the lumbar region, following slight trauma. Spontaneous hemorrhages into the pachydermatocele necessitated reoperation in 1907, 1911 and 1912. A spina bifida occulta and meningocele were present beneath the tumor.

Case 2—Reported by Carrington and Bullitt,³⁶ 1926

A 22 year old Negro laborer developed a hemorrhage into a tumor in the right flank. The tumor, originally as large as an orange, became, in the course of two hours, larger than the patient's head. Evacuation of the hematoma, six days later, was followed by healing.

Cases 3, 4, and 5—Reported by Heuer and Bell³⁷ 1931

Case 3—A 40 year old white man, as the result of a fall, developed a hematoma in a pachydermatocele on the left buttock. Spontaneous evacuation of the blood clot occurred, but the wound became infected and did not heal completely. When the acute infection subsided the tumor was excised but the patient died about three years later from a malignant growth arising from the right sciatic nerve.

Case 4—A 32 year old white man had a spontaneous hemorrhage into a tumor in the interscapular region. The patient had multiple subcutaneous tumors and scattered areas of skin pigmentation. After he felt something "break loose" within the tumor, he went into shock and died within 12 hours, apparently as the result of bleeding into the pachydermatocele.

Case 5—A 33 year old colored man complained of swelling of the side of his head of four days' duration. A mass as large as a grapefruit developed over the left temporal region. Evacuation of a hematoma in a gelatinous tumor beneath the temporal muscle was followed by satisfactory healing.

Case 6—Reported by Gordon,³⁸ 1932

A 44 year old white man had, at the ages of 24 and 32, developed hematomata in a neurofibroma on the right cheek. Three weeks before he was seen, he again struck his right cheek and a massive swelling occurred. The patient expired during operative removal of the hematoma and the greater portion of the tumor. Autopsy showed a number of tumors in the dura mater, in the substance of the right cheek, in the anterior wall of the stomach, and along the abdominal sympathetic nerve trunks.

Case 7—Reported by Brunner,³⁹ 1936

A 32 year old hotel employee had a spontaneous hemorrhage into a large tumor on the right buttock. After evacuation of the hematoma, rapid growth occurred in the tumor (malignant change?).

SUMMARY AND CONCLUSIONS

The manifold aspects of multiple neurofibromatosis have been reviewed in brief, with illustrations from our experience, and two of our cases with unusual surgical complications have been reported in detail. In controlling this disease we are impressed with the need of recognizing that the condition frequently is hereditary, that individuals showing the slightest evidence of involvement should be informed of the familial nature of the malady, and that they should also be advised against having children. There is a definite need to recognize and to study the mild type of the disease. More detailed studies of families so affected may help to determine the mode of its transmission.

The surgical complications in neurofibromatosis should be recognized early and appropriate treatment instituted.

These complications fall readily into three groups. The first is illustrated by those patients with complaints resulting from pressure of neurofibromata upon important structures. Whenever possible, these benign growths should

be removed. The second consists of those individuals who develop a malignant lesion at one or more points along a nerve trunk. Although there is no satisfactory treatment of these malignant growths, radical extirpation of the tumor (or amputation) followed by supplementary roentgenotherapy is the procedure usually advised. Into the third group fall those cases of neurofibromatosis with hemorrhage into a pachydermatocele. The treatment of choice is to administer adequate transfusions, evacuate the hematoma and remove the gelatinous tumor into which the bleeding has occurred.

BIBLIOGRAPHY

- ¹ van Bogaert, Ludo. Les Dysplasies Neuro-ectodermiques Congénitales. *Rev Neurol*, **63**, 353-398, 1935
- ² (a) Osler, W. On a Family Form of Recurring Epistaxis Associated with Multiple Telangiectases of the Skin and Mucous Membranes. *Johns Hopkins Hosp Bull*, **12**, 333-337, 1901
(b) Dickson, W. E. C. Certain Intracranial Tumors, Their Variability and Multiplicity. *Brit Med Jour*, **2**, 1016-1018, 1933
- ³ (a) Fischer, G. A. Studien über Vererbung von Hautkrankheiten, die Nachkommenschaft der Recklinghausenkranken. *Arch f Dermat u Syph*, **152**, 611-616, 1926
(b) Sharpe, J. C., and Young, R. H. The Clinical Manifestations in Thirty-One Cases of von Recklinghausen's Neurofibromatosis. *Arch Int Med*, **59**, 299-328, 1937
- ⁴ Preiser, S. A., and Davenport, C. A. Multiple Neurofibromatosis (von Recklinghausen's Disease) and Its Inheritance with Description of a Case. *Am Jour Med Sci*, **156**, 507-540, 1918
- ⁵ Leers, H. Recklinghausensche Krankheit und cerebrales Syndrom bei einem hochstwahrscheinlich einigen Zwillingspaar. *Ztschr f menschl Vererb-u Konstitutionslehre*, **19**, 721-730, 1936
- ⁶ Turner, O. A., and Gardiner, W. J. The Familial Involvement of the Nervous System by Multiple Tumors of the Sheaths and Enveloping Membranes. An Hereditary, Clinical and Pathologic Study of Central and Peripheral Neurofibromatosis. *Am Jour Cancer*, **32**, 339-360, 1938
- ⁷ Hockstra, G. Über die Familiäre Neurofibromatosis mit Untersuchungen über die Häufigkeit von Heredität und Malignität bei der Recklinghausenschen Krankheit. *Virchows Archiv*, **237**, 79-96, 1922
- ⁸ Harbitz, F. Family with Multiple Neurofibromatosis (von Recklinghausen's Disease). *Norsk mag f laegevidensk*, **99**, 609-615, June, 1938
- ⁹ Frets, G. P. The Hereditary Aspect of Five Cases of von Recklinghausen's Disease. *Genetica*, **11**, 347-366, 1928-1929
- ¹⁰ Struwe, F., and Steuer, E. J. Eine Recklinghausen Familie. Klinische und anatomische Untersuchungen. *Ztschr f d ges Neurol u Psychiat*, **125**, 748-790, 1930
- ¹¹ Smith, Robt. W. A Treatise on the Diagnosis and Treatment of Neuromas. Hodges and Smith, Dublin, 1849. See also Fulton, J. H. *New Eng Med Jour*, **200**, 1929
- ¹² Thompson, Alexis. On Neuroma and Neurofibromatosis. Turnbull and Spears, Edinburgh, 1900
- ¹³ Spittel, R. L., and Fernando, S. E. A Case of Elephantiasis Neuromatosa. *Brit Med Jour*, **1**, 596-597, 1929
- ¹⁴ Dandy, W. E. Surgery of the Brain. Practice of Surgery, Dean Lewis, Vol. XII, W. F. Prior & Co., Hagerstown, Md., 1932
- ¹⁵ Kernohan, J. W., and Parker, H. L. A Case of von Recklinghausen's Disease with Observations on the Associated Formation of Tumors. *Jour Nerv and Ment Dis*, **76**, 313-330, 1932
- ¹⁶ (a) Katzenstein, R. Über innere Recklinghausensche Krankheit (Endotheliom,

- Neurinome, Gliome, Gliose, Hydromyeli) Virchows Arch f path Anat, 286, 42-61, 1932
- (b) Penfield, W, and Young, A W The Nature of von Recklinghausen's Disease and of the Tumors Associated with It Arch Neurol and Psychiat, 23, 320-344, 1930
- ¹⁷ Cushing, H, and Eisendrath, L Meningiomas, Their Classification, Regional Behavior, Life History and Surgical End-Results Chas C Thomas, Baltimore, Md, 1938
- ^{17a} Verocay, J, and Masson, P cited by Cushing, H, and Eisendrath, L ¹⁷ Vide supra Chap I, pp 15-17
- ¹⁸ Penfield, W Cytology and Cellular Pathology of the Nervous System Paul B Hoeber, New York, 1932
- ¹⁹ Heuer, G J Ein Fall von Ausgedehntem schwammhosenartigem Naevus pigmentosus pilosus congenitus mit Hamatom des Ruckens und Spina Bifida occulta Seine Bezeichnung Zur v Recklinghausenschen Krankheit Beitrag z Klin Chir, 104, 388-426, 1917
- ²⁰ Stalman, A Nerven-, Haut- und Knochenveränderungen bei der Neurofibromatosis Recklinghausen und ihre entstehungsgeschichtlichen Zusammenhänge Virchows Arch f path Anat, 289, 96-126, 1933
- ²¹ Brooks, B, and Lehman, E P The Bone Changes in Recklinghausen's Neurofibromatosis Surg, Gynec, and Obstet, 38, 587-595, 1924
- ²² Cohn, I Epithelial Neoplasms of Peripheral and Cranial Nerves Report of Three Cases and a Review of the Literature Arch Surg, 17, 117-160, 1928
- ²³ Tucker, B von Recklinghausen's Disease with Especial Consideration of the Endocrine Connection Arch Neurol and Psychiat, 11, 308-320, 1924 Discussion of this presentation by Dr H Cushing
- ²⁴ Wakeley, C P, and Parkes-Weber, F Generalized Neurofibromatosis with Naevus Anaemicus Internat Clin, 1, 44-47, 1936
- ²⁵ (a) Sharpe, J C, and Young, R H Neurofibromatosis The Effect of Pregnancy on the Skin Manifestations J A M A, 106, 682-683, 1936
- (b) McNally, H B Pregnancy Complicating Neurofibromatosis with Associated Intrathoracic Tumor Amer Jour Obstet, 33, 501-502, 1937
- (c) Frunsholz, A, Louyot, J, and Richon, J Neurofibromatose Generalisee (Maladie de Recklinghausen) et Gestation Presse med, 43, 1449-1452, 1935
- ²⁶ Jackson, A H Three Cases of Multiple Neurofibromatosis with Malignant Degeneration Jour Nerv and Ment Dis, 78, 581-596, 1933
- ²⁷ Craig, W M Pain Associated with Neurofibromatosis Surg Clin N Amer, 6, 1365-1379, 1926
- ²⁸ Ferreri, G Neurofibroma of the Pharynx in a Case of Recklinghausen's Disease Riv oto-rino-oftal, 3, 52, 1926
- ²⁹ Moniz, E Recklinghausen's Disease Large Neurofibroma of the Tongue Rev Neurol, 39, 222-225, 1923
- ³⁰ Heuer, G J, Andrus, W D W, and Taylor, A Surgery of the Thorax Nelson's System of Surgery, Vol IV, Chap V, Thos Nelson and Sons, New York, 1932
- ³¹ Miller, A Neurofibromatosis, with Reference to Skeletal Changes, Compression Myelitis and Malignant Degeneration Arch Surg, 32, 109-122, 1936
- ³² Smith, F R Neurofibroma of the Ovary Associated with Recklinghausen's Disease Am Jour Cancer, 15, 859-862, 1931
- ³³ McDonnell, C H Neurofibromatosis of Bladder and Prostate Am J Surg, N S, 34, 90-93, 1936
- ³⁴ (a) Adrian, C Die Multiple Neuromatose (Recklinghausensche Krankheit) Centralb f d Grenzgeb d med u chir, Jena, 1903 Quoted by Heuer, G, et al ³⁰
- (b) Garre, C Über Sekundaer Maligne Neurome Beitrag z klin Chir, 9, 465, 1892
- (c) Hosoi, K Multiple Neurofibromatosis (von Recklinghausen's Disease) with Especial Reference to Malignant Transformation Arch Surg, 22, 258-281, 1931

- ³⁵ Stewart, F W, and Copeland, M M Neurogenic Sarcoma Am Jour Cancer, 15, 1235-1320, 1931
- ³⁶ Carrington, G L, and Bullitt, Jas B Hemorrhage in a Case of von Recklinghausen's Disease J A M A, 87, 166-167, 1926
- ³⁷ Heuer, G J, and Bell, H G Hemorrhage into and Infection of Large Tumors (Pachydermatoceles) of von Recklinghausen's Disease ANNALS OF SURGERY, 95, 15-24, 1931
- ³⁸ Gordon, S Hemorrhage Complicating von Recklinghausen's Disease Canad Med Assn Jour, 27, 524-525, 1932
- ³⁹ Brunner, W Elephantiasis Neuromatodes Deutsch Ztschr f Chir, 246, 751-759, 1936
- ⁴⁰ Stern, E L The Intraspinal Injection of Vitamin B Am Jour Surg, N S, 39, 495-511, 1938

DISCUSSION—DR GEORGE J HEUER (New York, N Y) Doctor Hart in his interesting discussion of von Recklinghausen's disease has grouped the surgical complications of this condition as those arising from hemorrhage into the large, so-called pachydermatoceles, from tumors, usually neurofibromata, implicating or compressing important structures in the various cavities of the body and of the extremities and from malignant degeneration of certain of the tumors occurring in this disease With regard to the first named complication, we were the first, I believe, to describe an instance of recurring, serious hemorrhage into the large tumors of von Recklinghausen's disease, and since this original observation, have seen three additional examples The seriousness of this complication is illustrated by our experience, for of the four cases, one died from hemorrhage into the tumor and one had such serious hemorrhages that blood transfusions alone saved his life The nerve tumors of the neurofibroma group may, of course, occur along the course of intracranial, spinal or peripheral nerves, and not infrequently they give rise to symptoms which require surgical removal of the tumors for their relief Both these tumors and the skin tumors seen in von Recklinghausen's disease may undergo malignant change, although this complication is rare in my experience Such malignant tumors present the same indications for treatment as other tumors

A serious complication in this disease, to which Doctor Hart has not referred, is infection in the large tumors (pachydermatoceles) of von Recklinghausen's disease If one is familiar with the curious myxomatous tissue making up these tumors, he can visualize the rapidity of spread of an infection and the difficulties, surgically, of coping with it We have observed one case The patient developed a small ulcerated area of the skin over a pachydermatocoele, presumably the portal of entrance of the infection The infection spread throughout the large tumor with great rapidity Its size increased greatly, the skin over it became red and hot, the entire tumor was tender For 35 days, the patient's temperature was elevated, rising at times to 106° F, his pulse rose to 144, his leukocytes varied between 25,000 and 40,000 He was, throughout the period, very ill At no time did the infection proceed to abscess formation, and fortunately, after a serious siege of illness, the patient recovered

As another, perhaps unique, observation in this disease, I should like to record the occurrence of a large myxomatous tumor within the thorax in all respects similar to the large external pachydermatoceles The patient, a woman, age 41, entered the New York Hospital complaining of pain in the chest and shortness of breath She presented the three major characteristics of von Recklinghausen's disease, pigmentation of the skin, skin tumors of the

fibroma molluscum type and subcutaneous tumors of the extremities believed to be neurofibromata. Roentgenograms of the chest showed an enormous shadow which completely occupied the right hemithorax except for a small area at the apex. The heart and mediastinum were dislocated to the left. A diagnosis of intrathoracic lipoma was made and operation performed March 16, 1939. On exposure, the huge tumor appeared to be encapsulated but the supposed capsule proved to be the visceral pleura. The pleura was split and the tumor within it completely removed. It weighed $8\frac{1}{2}$ pounds and measured $34 \times 29 \times 10$ cm. in its various diameters. It was composed of gelatinous, myxomatous tissue resembling that seen in the external pachydermatocles of von Recklinghausen's disease. Dr. N. C. Foot describes the microscopic appearance of the tumor as follows: "A Cajal impregnation of this enormous tumor is extremely interesting as it brings out the morphology of the myxoblasts in the most unusual fashion. Microscopic fields which show only small nuclei in the ordinary H and E and Masson stains, show in these impregnated sections a profusion of stellate and spider-like myxoblasts which anastomose with one another and have a startling resemblance to the spider-cells seen in the central nervous tissue. There are, however, no nerve fibers or anything to indicate true nervous origin of this tumor. Many of these cells send anastomosing processes around the capillaries in exactly the same manner as those seen in the astrocytes of the brain. The results with the Cajal impregnation indicate that this tumor is more in the nature of a rather undifferentiated myxoma than a myxosarcoma." This patient has made a satisfactory recovery.

DR KELLOGG SPEED (Chicago). As outlined by Doctor Hart, this disease is very easily overlooked by physicians, but I may add, more easily recognized by dermatologists. The patients usually seek surgery on account of the size or position of one of the tumor masses which may involve a large nerve trunk by invasion pressure or present cosmetic complications. In the differential diagnosis, I have met stumbling blocs in an effort to distinguish between fibroma or fibromyxoma of the extremities, supernumerary nipples, periosteal fibrosarcoma, cystic osteitis and retroperitoneal tumors with myxomatous characteristics.

At the Presbyterian Hospital, Chicago, and from my own records, I may report 14 instances of von Recklinghausen's disease, five with definite familial history, three with sarcomatous degeneration of one area, three involving bone changes, one mistaken for periosteal fibrosarcoma and one cystic in type, recurring slowly after two attempts at removal locally. Autopsy was performed upon two patients, with findings of metastases (after sarcomatous degeneration) in lungs and vertebrae. In two of my own fatal cases, the disease, having become malignant in the thigh, invaded the peritoneal cavity and spread via the periaortic lymph channels, proving that the peritoneal, as well as the thoracic or cranial cavity may become involved. Errors in diagnosis seem to follow incomplete examination of the patient's fully bared body. I am also convinced that many of the unclassified retroperitoneal tumors, malignant and possibly myxomatous in consistency, take origin from unrecognized neurofibromatosis.

DR MAX M. PEET (Ann Arbor, Mich.). I wish to add one note of the very interesting intracranial complications which may occur with von Recklinghausen's disease. We all know of the rather frequent occurrence of neurofibromata on the eighth nerve, and also the association with meningiomata. Other types of tumors of the central nervous system may also be associated with von Recklinghausen's disease. We had one patient who, in addition to

generalized peripheral neurofibromata, had acoustic tumors, and a very large meningioma in the occipital region with evidences also of meningiomata of the spinal cord. This patient died from pneumonia, and at autopsy, 17 meningiomata were found along the course of the spinal cord and numerous intracerebral and spinal gliomata. Dr Percival Bailey, in studying the sections, found every known type of tumor involving either the central nervous system or the peripheral nerves that he had ever seen. The patient had every type of glioma. In fact, inside of certain large gliomata, in this brain were other gliomata of an entirely different character. In other words, this man had every type of tumor that could occur peripherally or centrally in the nervous system. We have seen two similar cases since.

DR EDWIN R SCHMIDT (Madison, Wis.) I wish to add six other cases, that are being reported elsewhere. In this subject, I should like to call attention to a thing which the speakers have brought out, namely, the importance of recognizing the *café au lait* spots in early cases, because the large number of cases that are being reported are usually late, when pressure symptoms have manifested themselves and surgery is difficult.

These six cases have all started in the optic nerve, and there has been great difficulty in making an early diagnosis. If the diagnosis is made earlier, then surgery is going to be more effective.

DR DERYL HART (closing) Doctor Schmidt brought up the matter of early diagnosis. I think the most important single factor in the control of neurofibromatosis is early diagnosis, so that we can impress upon the patients the familial character of the condition and to urge upon them the undesirability of passing this on as will occur if they have children.

THE EFFECT ON THE BONE MARROW OF DISRUPTION OF THE NUTRIENT ARTERY AND VEIN*†

CHARLES HUGGINS, M D , AND EUGENE WIEGE, M D

CHICAGO, ILL

FROM THE DEPARTMENT OF SURGERY OF THE UNIVERSITY OF CHICAGO CHICAGO ILL

THE NUTRIENT VESSELS in the shaft of the femur in rabbits were disrupted at operation and the bone marrow studied at subsequent time intervals of four to 88 days. The nutrient vessels are relatively small and are vulnerable to injury by trauma and operation. The sequelae of such an injury and the nature of repair in the marrow have not been described.

One of the theoretic considerations in these experiments was the comparison of the extent and position of the necrosis with the natural central fat core pattern of the femur. In the extremities of man, the dog, the rabbit, and other mammals, there is frequently seen a pattern consisting of a large central core of yellow marrow surrounded by a peripheral bark of red marrow in contact with the bone,¹ this pattern is seen in regions of centripetal marrow regression in normal growing and adult animals, most frequently in the shaft of the femur, and its cause is unknown.

The blood supply of the femur in the rabbit has the usual small epiphyseal and periosteal arterial twigs, and in addition three arteries supplying the shaft. The largest of these, the main nutrient artery of the shaft, arises from the lateral circumflex artery near its origin from the femoral artery.² It courses downward and posteriorly to enter the nutrient foramen on the medial aspect a short distance below the lesser trochanter just anterior to the dense tendinous insertions of the short adductor muscles. Moore and Corbett³ stated that ligation of the nutrient artery diminished the amount of callus in experimental fractures, but this was denied by Houang,⁴ who found that fractures healed as well after section of the nutrient artery as in the control limb. Johnson,⁵ in an ingenious series of experiments on the tibia in dogs, found that the nutrient arteries are the most important osseous vessels and maintain viability in the medulla and inner half of the cortex. Kistler² injected large carbon particles into the nutrient artery, producing severe infarction of the marrow with subsequent connective tissue reaction. He found that interference with the blood supply to the femur in rabbits by rupture of one or more nutrient vessels did not produce infarcts or stimulate reactionary changes except in one rabbit. Brunschwig⁶ elevated the periosteum between the epiphyseal plates, thus severing all blood supply and drainage, in growing dogs this resulted in extensive marrow infarction in the shaft, but in adult dogs with closed epiphyseal plates infarction was not observed.

* Aided by grants from the Fenger Memorial Fund and the Douglas Smith Foundation for Medical Research

† Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

Method—In 18 rabbits, seven adults and 11 with open epiphyses, the main nutrient vessels of the femur were interrupted 23 times, under ether anesthesia and aseptic precautions. An incision, 3 cm in length, was made just below the inguinal ligament, the quadriceps muscle, just lateral to the femoral vessels and nerve, was separated in the direction of its fibers by blunt dissection until the femur was reached. The principal nutrient vessels were easily seen just anterior to the tendinous insertion of the short rotator muscles just below the lesser trochanter and interrupted either by ligature or rupture with a forceps, the nutrient canal was then inspected for completeness of operation. Closure was obtained by means of a continuous silk suture in the skin.

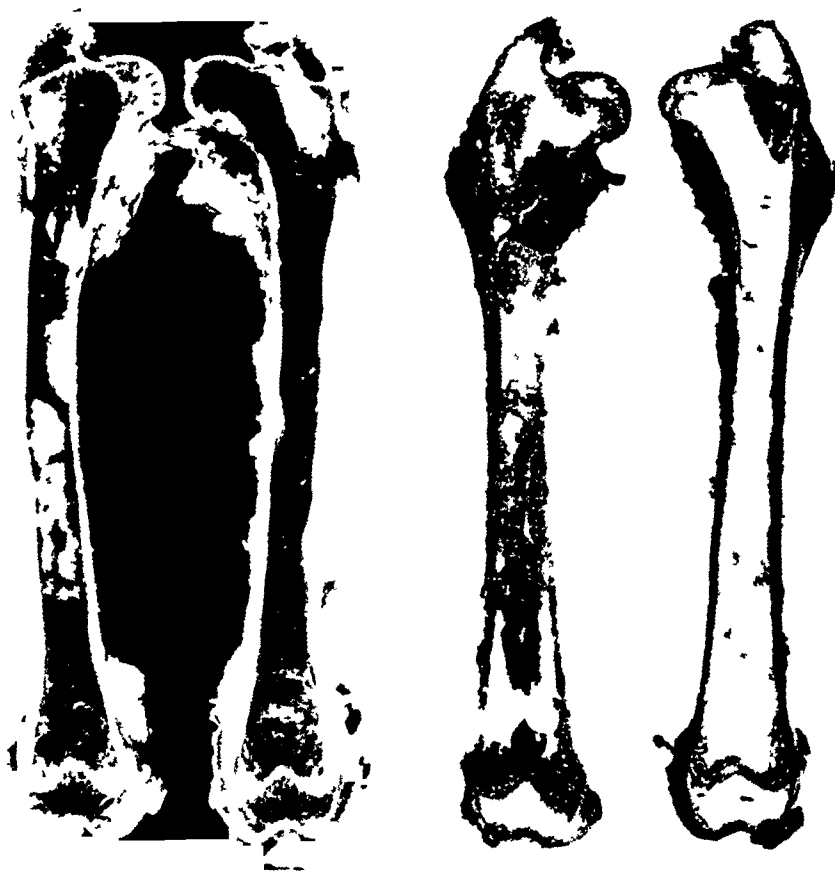


FIG 1—Necrosis in marrow following disruption of the principal nutrient artery. From left to right the specimens are the experimental and control femora of Rabbit 1180 at four days and similar specimens from Rabbit 1240 at seven days. Injected with ink one day before necropsy.

From three to 84 days later, 15 rabbits were injected intravenously with colloidal solutions which accumulated in the macrophages, proving the extent of revascularization. Nine rabbits were injected with a freshly prepared 20 per cent solution of Higgins' American India ink in 0.9 per cent NaCl, using 20 cc on two consecutive days before necropsy. Three rabbits were injected with 5 cc doses of thorotrast (25 per cent thorium dioxide by weight) on each of three consecutive days before death. Three rabbits were injected with carbon on the third and fourth postoperative day and with thorium dioxide two to three weeks later to show the amount of vascular supply on each of these occasions.

TABLE I

Rabbit Number*	Days Since Operation	Extent of Necrosis in the Gross†	Microscopic Findings in Transverse Sections
12-C	4	Small	Engorged capillaries at the periphery, coagulation necrosis in middle of femur
104-O	4	Large	This rabbit received colloidal carbon injections on the fourth day and thorium on the thirteenth day. A large carbon-free area and a small thorium-free zone show that on the fourth day there was much ischemia, which had disappeared by the thirteenth day.
112-O	4	Large	Much pale-staining necrosis involving center and large part of periphery of marrow
118-O	4	Large	Most of the area is necrotic with a partial rim of living marrow. The necrotic area is pale staining and contains no carbon. There is a slight breakdown of cells with nuclei disappearing. Slight phagocytosis.
11-O	6	Small	Much more necrosis than appears in the gross. Much extravasation of blood between the necrotic fat cells and capillary engorgement around the periphery of necrosis. Fat cell nuclei appear normal. Many small macrophages.
124-O	7	Very large, reaching to epiphyseal plate	The necrotic marrow is pale staining with pyknotic nuclei and much basophilic nuclear debris.
79-C	7	Large necrotic areas in upper and lower thirds separated by living marrow	Coagulation necrosis. Macrophages and many other hemopoietic cells are creeping in at the periphery of the necrosis.
77-C	9	Large	Rim of living marrow surrounds the necrotic center which is being invaded by capillaries and macrophages.
125-O	11	Small, located in distal third of bone	Necrosis reaches the periphery of the bone at one point, it is being invaded from the side by new capillaries, myelocytes are forming.
108-O	11	Two small necrotic areas, one near nutrient canal, other in lower third	Peripheral invasion by new capillaries.
24-C	11	Small, near nutrient canal	
120-O	11	Large	Pale-staining cells with protein fibrils in necrotic areas. Intense peripheral capillary congestion.

TABLE I (Continued)

Rabbit Number*	Days Since Operation	Extent of Necrosis in the Gross	Microscopic Findings in Transverse Sections
104-O	13	None	About 80 per cent of the section is gelatinous marrow involving the center and all of the periphery except a semilunate area. Many foreign body giant cells.
115-C	14	Small	Two small areas of necrosis with pale cells. Much gelatinous marrow.
112-O	22	None	Injected with carbon and thorium. Nearly normal marrow throughout. At the periphery there is much carbon as compared with the center. Much thorium throughout.
19-C	28	None, large exostosis at site of nutrient canal	Normal appearance. There is a large clump of vacuolated cells with small fat globules, young fat cells.
14-C	29	None	Normal except for bone island in marrow near nutrient canal.
113-O	30	None	Normal appearance throughout, as in opposite control, except there is a small island of bone in the marrow center near nutrient canal.
100-O	74	None, large exostosis at site of nutrient canal	Normal appearance.
120-O	74	None	Normal except for small bone area in marrow center.
115-C	77	None	Normal appearance.
13-C	80	None	Normal appearance.
12-C	88	None	Normal appearance.

* The letters, -O, -C, designate open and closed epiphyseal cartilage plates

† "Small" indicates an area of necrosis less than one-third of the transverse area of the marrow

The bones were fixed in 10 per cent formalin, decalcified in 5 per cent nitric acid and sectioned transversely with a razor blade in 5 Mm slices. Histologic sections were stained with hematoxylin-eosin.

Results—The findings are shown in Table I. In the gross, marrow necrosis could be seen as an opaque yellow area in all specimens at 11 or less post-operative days, and in one specimen, 14 days after operation. The nutrient canals were all found to be occluded and recanalization was not observed. In all specimens later than 22 days after vascular interruption, the marrow appeared in the gross similar to that in the contralateral unoperated femur. The extent of the necrosis was variable. In the series less than 12 days, the necrosis was small five times and large seven times. In three cases, the marrow infarction was discontinuous, consisting of two necrotic zones in the shaft separated by normal marrow.

The center of the marrow was involved in the necrosis to a greater extent than the periphery. In no case was the entire transverse section of the marrow necrotic and there was always at least a partial rim of living marrow adjacent to the bone in some part of the section. The necrosis, however, was not confined to the center of the marrow and in every case involved the periphery of the marrow reaching to the bone in at least one area. In three cases, these were teat-like exostoses containing marrow at the site of the old nutrient canal. No other osseous changes were detected.

On microscopic examination, the necrosis was characterized by pale-staining cells, whose outline was maintained for about one week, and later, a pyknotic appearance of the nuclei with accumulation of small basophilic bodies resembling nuclear debris. There was a complete absence of inflammatory exudate. The spaces between fat cells early became filled with a fluid rich in protein, staining like fibrils. In most of the sections there was an intense capillary engorgement in the living marrow adjacent to the necrosis. Megakaryocytes and fat cells stained well, longer than other cells in the necrotic zones, but shrunken nuclei were evidence that these cells were dead. The specific leukocyte granules persisted longer than their nuclear material, especially in the eosinophile series.

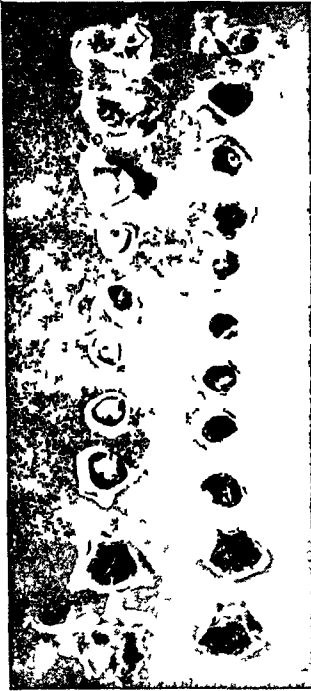


FIG 2—Transverse sections showing marrow necrosis following nutrient vessel interruption at nine days (Rabbit 77 C). Left, the infarcted marrow, right, the unoperated control.

Recovery was apparent four days after operation. The first apparent sign was infiltration of the periphery of the necrosis with more or less radially arranged new capillaries and macrophages. The central part of the necrosis was the last to persist and remained free of the injected particulate matter longest. Along with the new capillary and macrophage infiltration (Figs 3 and 4), many other marrow cells and many multinucleated foreign body giant cells infiltrated the periphery of the necrosis. There was only slight histologic evidence of the disposal of necrotic marrow by the invading new tissue by phagocytosis, and few phagocytes contained unclear material. There was no evidence of lysis. An interesting finding was a lack of fibroblast formation.

From the thirteenth to the twenty-second day after operation, there were seen large areas of gelatinous marrow, an edematous loose fibrillar bone marrow (Fig 5) with isolated single or small clumps of hemopoietic cells in comparison to densely accumulated clumps of myelopoietic cells seen in the normal condition. This gelatinous marrow was not seen after the twenty-eighth day and may be interpreted as a replacement stage in bone marrow formation. Small islands of bone occurred in the marrow substance in three specimens at 29, 30, and 74 days, this bone was located in the neighborhood of the nutrient

DISRUPTION OF CIRCULATION OF BONE

FIG 3—The junction of the mic marrow infarct (upper left) with normal marrow (Rabbit 110) six days ($\times 105$)

FIG 4—The junction of the marrow infarct with normal marrow at 11 days (Rabbit 1250) showing invasion by new capillaries, macrophages and myelocytes. India ink injected one day before death ($\times 325$)

FIG 5—The fatuous marrow stage of marrow repair after nutrient artery disruption at 13 days (Rabbit 1040). Normal marrow is seen in the lower left corner ($\times 115$)

canal Since bone is consistently absent from the marrow of the shaft of the rabbit femur, this finding is of significance

Discussion—Necrosis of the bone marrow always occurred following interruption of the main nutrient vessels While the same general appearance obtained, there were quantitative differences in the rabbits Differences in the extent of necrosis undoubtedly can be related to differences in periosteal and articular blood supply in individual femora The location of the necrosis shows well the area of bone marrow supplied by the nutrient artery, which is mainly the center of the marrow A theory that the central fatty core of normal extremity marrow is related to decreases in nutrient artery function is thus supported in part by the findings, but a discordant note is struck by the observation that the necrotic area always reaches the bony wall at one point

In all cases, complete repair occurred in the bone marrow Study of the nature of the reparative process was enhanced by the use of injected colloids, showing vascularity at certain time intervals Bone marrow necrosis was found to repair by a creeping substitution process from the peripheral living marrow Between nine and 28 days, the presence of gelatinous marrow indicates incomplete regeneration of bone marrow At 74 days and later, the marrow itself was found completely repaired and indistinguishable from the normal There was a striking absence of inflammatory reaction to the necrosis

The conspicuous absence of fibroblasts is of interest and may be contrasted with the findings of Kistler, who used carbon emboli, producing a much more chronic process with much fibrosis of the marrow The necrosis occurring after simple nutrient vessel disruption apparently is a more bland process of injury than the small carbon emboli used by Kistler, which evidently obstructed smaller vessels in a diffuse manner The repair of these marrow infarcts stands also in contrast to the repair of the infarcted spleen, an organ likewise rich in macrophages Bloom and Tahaferio⁷ found that the infarcts in the malarial spleens of canary were repaired by a process of macrophage infiltration, inflammation, scar tissue formation, and finally proliferating lymphocytic nodules formed The inflammatory and scar stages were not observed following nutrient artery interruption in our experiments

CONCLUSIONS

Surgical interruption of the principal nutrient artery and vein in the rabbit was always followed by bone marrow necrosis The amount of necrosis varied in extent, the central marrow and a part of the periphery adjacent to bone were always involved There was total absence of inflammatory exudate An infiltrating type of repair by new capillaries and macrophages arising from the living marrow at the periphery of the necrotic zone was apparent four days after ligation, and no necrotic masses remained after 22 days Only slight evidence of removal of the necrosis by phagocytosis was obtained The earlier marrow repair was characterized by loose isolated cells in an edematous gelatinous marrow, but after 70 days, the marrow was indistinguishable from normal The absence of scar tissue in the reaction to the necrosis was striking

REFERENCES

- ¹ Huggins, C Anat Rec , 74, 231, 1939
- ² Kistler, G H Arch Surg , 29, 589, 1934
- ³ Moore, J E, and Corbett, J F Surg , Gynec and Obstet , 19, 5, 1914
- ⁴ Houang, K Presse méd , 42, 2074, 1934
- ⁵ Johnson, R W Jour Bone and Joint Surg , 9, 153, 1937
- ⁶ Brunschwig, A Proc Soc Exper Biol and Med , 27, 1049, 1930
- ⁷ Bloom, W , and Tahaferro, W H Jour Infect Dis , 63, 54, 1938

CHONDRITIS OF KNEE*

WILLIAM DARRACH, M D

NEW YORK, N Y

FAILURE to cure internal derangement of the knee by removing a meniscus through a small incision, has impressed on a good many surgeons the wisdom of using an incision large enough to explore the knee joint more thoroughly. Out of 376 arthrotomies for this condition 27.1 per cent were found to have an abnormal meniscus as the only lesion. In 15 per cent the anterior cruciate ligament has been found to be partially or completely ruptured. Other common additional lesions were hypertrophied fat pads, loose bodies, synovial changes and hypertrophic spurs. There were four negative explorations.

The most commonly associated condition in this type of knee has been an alteration of the articular cartilage covering the femur, patella and tibia. The first evidence seen is a change in color and firmness. Instead of a bluish white, the cartilage looks yellow. It feels softer when pressed with a blunt instrument and when the latter is moved along the surface, the cartilage will roll up in front of it. Later it becomes fissured and frayed and tongue-like processes can be lifted up. Detached small fragments will be found lying about the joint cavity, or larger pieces up to two centimeters in diameter will be found, either free or partially attached. In the more advanced cases, the condyles or patella will be largely denuded of cartilage over small or large areas. Sometimes these areas will be covered with shining fibrous tissue, either smooth or granular in appearance.

In the large majority of instances this condition involves only the superficial portion of the articular cartilage and rarely does one see the underlying bone exposed. Occasionally, a large, deep crater is encountered, extending into the bone, and a corresponding loose body may be found somewhere in the joint. It would seem proper only to apply the term osteochondritis to this latter type, if at all.

The sites where this condition was found most frequently were, in order, the dorsal surface of the patella, the anterior surfaces of the femoral condyles, the surface just above the intercondyloid notch, the under surface of the femoral condyles, the side walls of the notch, and the upper surface of the tibia. The involved areas are usually found on opposed surfaces, i. e., patella and anterior surface of femoral condyles, or lower surface of the latter and tibia. Fifty-one per cent of the cases showed involvement of the articular cartilage. In 68 per cent of the cases where it was present it was the only demonstrable lesion.

The most frequently encountered associated lesions found were meniscus alone in 76, meniscus and torn cruciate ligament in 31, loose body in 18.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

meniscus and loose body in 14, cruciate ligament alone in seven instances. Among the less common lesions found were three benign tumors (lipoma of fat pad, hemangioma of fat pad and lipoma arborescens), rheumatoid arthritis in two cases and extensive adhesions in two instances.

When this condition has been found, it has been our custom to shave off with a knife or sharp gouge, the affected cartilage, leaving as smooth a surface as possible. In eight cases we have had the opportunity of seeing at a secondary operation the late result. In six instances the areas were covered with shining, fibrous tissue either smooth or granular, in one this had occurred in the original lesion but new areas had appeared and in the other the original areas had deepened and enlarged. When this condition exists the return to normal function is distinctly slower than in the cases without this complication. This applies especially to joint fluid.

Although 26 of the cases were found in patients under age 20, the average age of the chondritis cases was 33, as compared with an average age of 25 of the cases without chondritis.

Because of its frequent association with other traumatic conditions of the knee, because it usually only affects the superficial portion of the articular cartilage, and because it generally appears on two opposed surfaces, we believe that this lesion is a response to trauma rather than the result of a general condition or to some interference with the subjacent blood supply. The term chondritis, therefore, seems more suitable than osteochondritis.

DISCUSSION—DR KELLOGG SPEED (Chicago, Ill.) In my recent experience with 300 consecutive injuries of the knee, excluding fracture, there have been found, upon examination or by operation, 25 instances of osteochondritis of the knee including the dissecans type, presumably existing before the trauma sustained at the time of the complaint of injury. Sometimes this condition within the knee has been completely unknown to the patient. In other instances, I have believed, particularly in some situations where compensation was sought, that the patient was aware of a prior knee joint disability and awaited some accidental trauma to capitalize it.

The onset of osteochondritis may be insidious—my youngest patient was age 18, the oldest 62. The condition is often ushered in by sudden hydarthrosis, which seldom shows blood upon aspiration and which may subside under rest or immobilization. Sometimes locking and simulation of derangement of a semilunar cartilage may be an initial symptom. A careful roentgenologic examination may show loose bodies or those about to loosen, usually from the articular surface of the femur, but in some instances, in spite of the roentgenogram, operation may be undertaken under a diagnosis of semilunar cartilage injury and the true situation exposed only after the joint is opened for inspection—or overlooked if the incision is not large enough to show all the possibilities of changes within the joint.

The treatment may be nonoperative, where there are no free loose bodies which may impinge between joint surfaces. Immobilization for a few weeks may permit a quieting down of the synovitis and absorption of the effusion. Recurrence of symptoms usually occurs eventually. Lasting cure may be obtained by operation. The choice of approach to the joint may be governed by roentgenologic findings or the absence of freely moving, detached bodies within the joint. One must not make the error, however, of believing that

the roentgenograms ever tell 100 per cent of the story of bone or cartilage change—in my experience it averages about 40 per cent

For locally loose, and about to wander, pieces of cartilage-bone, a small incision, usually the Jones hockey-stick type, may suffice for removal of all threatening masses. If there are true loose and wandering bodies, bold exposure of the joint by a para- or midpatella incision may be used. For young and very active individuals or athletes, I really prefer the split patellar incision because it permits earlier and safer active use of the joint. If there are diffuse changes in the synovia with thickening, jelly-like joint contents with loose bodies and joint crepitus, I employ complete synovectomy followed by early postoperative passive and active motion. No knee joint thus treated by me has failed to be benefited in varying degrees. In the small, pure and early dissecans type, I do not believe in paring the cartilage edge as may be done in older and long standing instances. When great deformity and disabling pain persist in the joint, resection of the knee promises relief and increased use of the leg.

TREATMENT OF AVULSED SKIN FLAPS*

ALFRED W. FARMER, M.D.

TORONTO, CANADA

CASES of severe avulsion of skin occur frequently in civil practice. Four such instances are herewith reported with a new method of treatment. Three of these followed automobile accidents, and one a domestic winger injury.

Technic of Treatment—The method of treatment consists first in the *excision* of all the avulsed skin. The assistant treats the traumatized area in any way thought desirable. This usually consists in a thorough cleansing and débridement. The cleansing of the raw area is performed with aseptic rather than antiseptic fluids. Thus soap and water, and saline are the solutions of common choice. The avulsed skin is then treated by removal of all the subcutaneous fat. It is necessary to do this thoroughly, although it is a tedious procedure. Holding the skin on a firm, flat surface, the fat is removed by scraping, or by cutting with curved scissors, well into the dermis. The skin is then sewn accurately back into the position from which it was removed. Quilting sutures are used also and the graft is perforated with numerous small stab wounds. The primary dressing is of normal saline. Firm pressure is obtained by bandaging, and a plaster encasement insures immobility. The dressing is changed in ten to 14 days, unless there is some special indication for an earlier examination.

ABBREVIATED CASE REPORTS

Case 1—G. N., male, age 10, was admitted in June, 1936, following an automobile accident. There was a compound fracture of the fibula, near the ankle joint, and a very severe laceration of the soft tissues of the leg and lower third of the thigh. The skin and subcutaneous tissues from the junction of the middle and lower thirds of the thigh to the ankle joint were torn free from the deep structures. The skin was also lacerated and abraded. It was decided that the upper and lower portions might possibly live due to circulation through the upper and lower ends but that the superficial tissues from the knee to within three inches of the ankle had no chance to survive. They were therefore, removed. The area which was very dirty, was cleansed in a routine fashion. The skin and subcutaneous tissues, which had been removed were then made into a full thickness graft by careful excision of all the fat. This free graft was replaced in the same position from which it had been taken, sewn about the edges and fixed with quilting sutures. A drain was left in place as the whole area was very dirty on admission.

The postoperative condition is shown in Figure 1. A restricted plaster encasement was necessary because of the fracture. There was a considerable amount of infection but despite this a large part of the full thickness graft lived (Fig. 2). The superficial tissues of the lower third of the thigh died due to poor circulation from above. It was thought later that this skin also might have been made advantageously into a full thickness graft. This area was covered with partial thickness grafts and the final result is shown in Figures 3 and 4.

* Read before the American Surgical Association, Hot Springs, Ark., May 11, 1937.
13, 1939



FIG 1—Case 1 Immediate postoperative appearance The fenestrated, immobilizing plaster encasement was necessary because of a fracture



FIG 2—Case 1 Showing the appearance about ten days from the time of the accident



FIGS 3 and 4—Case 1 Front and side views of the final result

Case 2—This patient was operated upon in association with Dr W S Keith B M, female, age 7, was admitted in October, 1937, following an automobile accident in which she had sustained laceration of the soft tissues of the left leg. The skin



FIG 5—Case 2 Removal of the flap from the leg

and subcutaneous fat were separated from the deep tissues, from above the knee region to about three inches above the ankle. They had retained an attachment along the medial aspect of the leg only, over a width of about two inches. The loose tissues were



FIG 6—Case 2 Return of the flap in the form of a free, full thickness skin graft

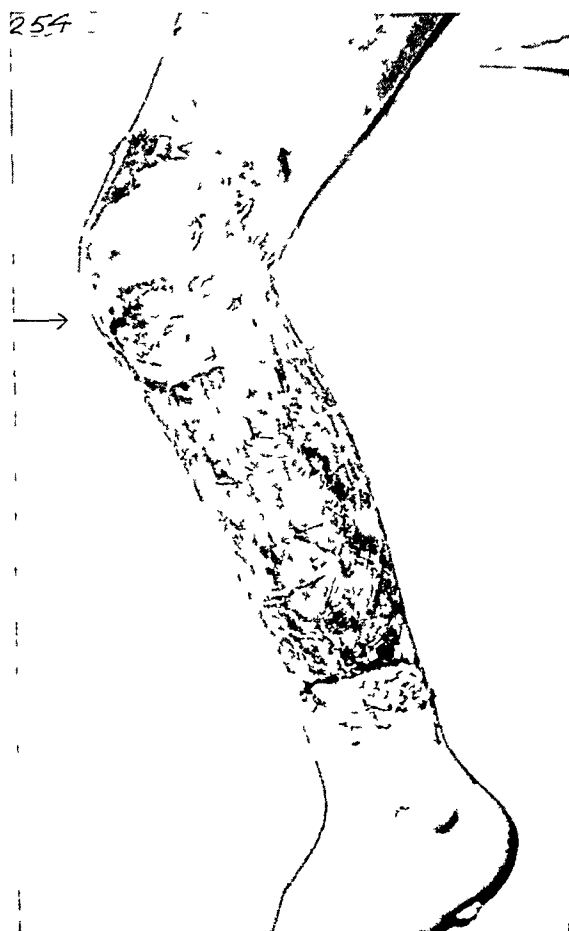


FIG 7—Case 2 The result two weeks after admission

AVULSION OF SKIN

cut free, where it was considered that they would not live if left in place (Fig 5) A full thickness free graft made of this skin was replaced exactly as removed (Fig 6) and sutured accurately into position Dressings were applied and left without disturbance



FIG 8—Case 2 Photograph taken two months after the accident

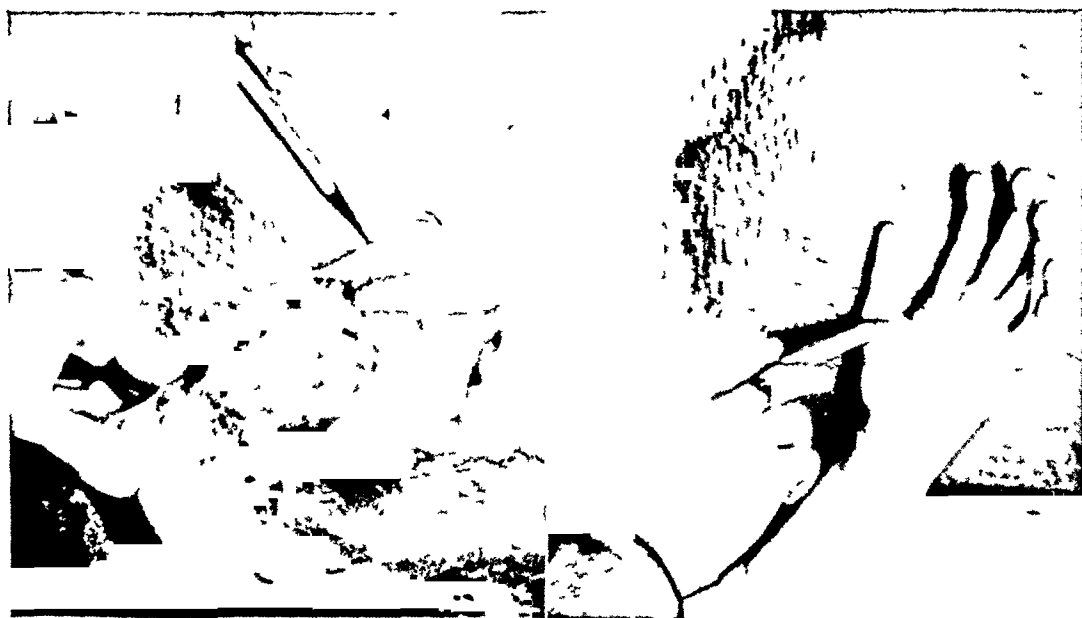


FIG 9—Case 3 Immediate postoperative result FIG 10—Case 3 The result six months after the accident

for two weeks There was practically a complete "take" of this graft, with the exception of one area (Fig 7, arrow) This was about one by two square inches in area and situated over the capsule of the knee joint The patient was discharged from the hospital in about three weeks from the time of her admission The result some months later is shown in Figure 8

Case 3—R B, male, age 10, was admitted in December, 1937, following a wringer injury. There was a laceration of the palm of the right hand, the skin, subcutaneous

fat, and fascia being separated from the deep tissues in the form of a flap, with its base above the wrist. This flap corresponded to about two-thirds of the area of the palm. The skin appeared very dirty and ragged, with no evidence of circulation, except in the immediate vicinity of the base. This patient was operated upon by the house surgeon in charge. After the usual cleansing and draping, the skin flap was removed beyond a point where circulation appeared adequate. All fascia and fat was scraped off, leaving a free full thickness graft, which was then reappplied to the hand and sutured in position. Firm pressure was applied over normal saline dressings. Because of the risk of infection in the very dirty wound, dressings were changed daily. There was a perfect "take." Figures 9 and 10 show the immediate post-operative and later results. On examination of the hand at the present time, it would be impossible to estimate the nature and severity of the original injury. The functional result is perfect.

Case 4—G H, male, age 18 months, was admitted in August, 1938, following an

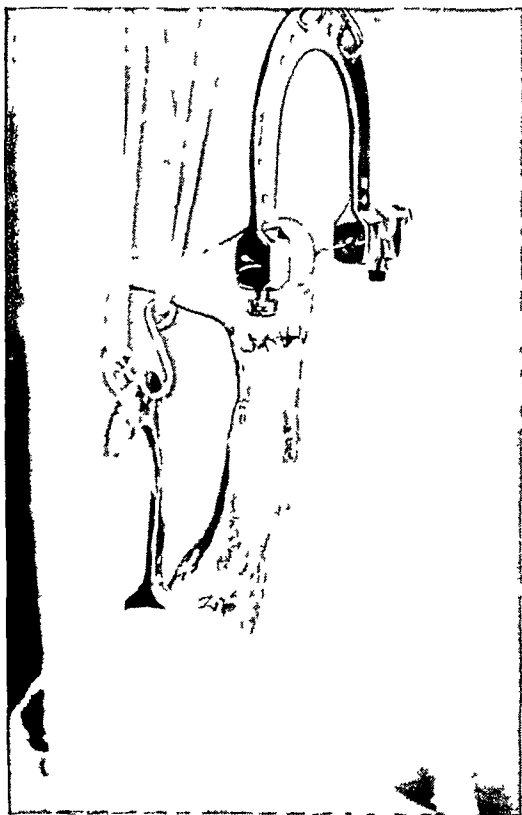


FIG 11—Case 4 The result two weeks after the accident

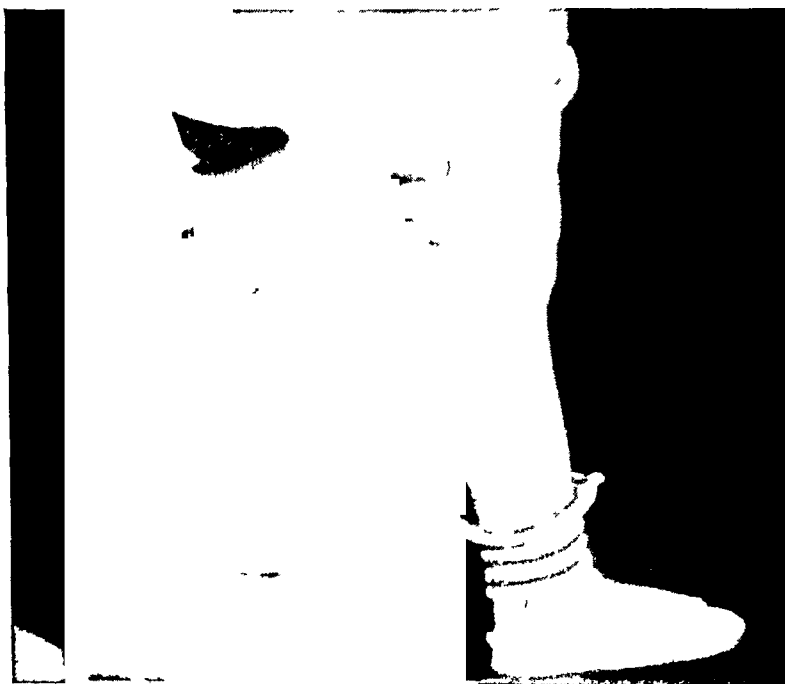


FIG 12—Case 4 The condition some months following the accident

automobile accident in which he sustained a fracture of both femora and a severe laceration of the left leg, extending from the knee to the ankle. The skin and subcutaneous fat were separated from the deep tissues, except on the anterolateral aspect, and at the ankle. The skin flap was cut free, leaving a small strip on the anterolateral aspect intact (part of this died). It was converted into a free full thickness graft and reappplied. The fractured fragments were controlled by skeletal traction. The nursing problem and general care was, of course, difficult. Despite this, over 80 per cent of the graft "took." The remaining raw area was later covered with a partial thickness graft. Figures 11 and 12 show the condition two weeks and some months, respectively, following the accident.

On examination of the literature, it is possible that this removal and replacement type of operation as described may have been performed previously, more by mistake than design, and with no comprehension of what took place. For instance, Malherbe,¹ in 1898, reported a case of scalp avulsion. The scalp was disinfected, shaved and sutured back in position. The peculiarity lies in the result. This was the only case of 21 of a similar variety, reported by Davis,² which did not slough. From the description, one might hazard a guess that possibly this free graft "took." The grafted scalp seemed to dry up and act as a dressing. There was some pulling away at the edges and healing was not complete for over three months. The record is not clear, and if there was a "take" of this free scalp graft, then the fact has not been recognized until the present. There is no reason why such a result should not be obtained, particularly if, in view of the present understanding, some modification of the graft were made.

This article does not undertake to discuss the preparation and after-care of a full thickness graft. This has already been done many times. The results obtained in accidental wounds depend chiefly upon the factor of infection. They will vary also to some extent, on associated injuries, which by their presence make the after-care of the graft more difficult.

SUMMARY AND CONCLUSIONS

Four cases are reported which illustrate the use of full thickness grafts as a primary measure in the treatment of accidents when a loss of superficial tissue seems inevitable. This type of graft gives a much better result than can be obtained with partial thickness grafts employed at a later date.

This method of treatment, besides saving the damaged tissues from certain death, saves also much hospitalization and gives a better cosmetic and functional result than by any other method.

REFERENCES

- ¹ Malherbe, A. *Bull. Med.*, 12, 1121-1123, 1898.
- ² Davis, J. S. *Johns Hopkins Hosp. Rep.*, 16, 257-362, 1911.

DISCUSSION —DR JOHN HOMANS (Boston). I am particularly interested in this contribution of Doctor Farmer's, because it applies very well to the sort of plastic work which I, as an ignorant plastic surgeon, have been performing. I have been making very wide flaps indeed, in trying to remove the subcutaneous tissues in elephantiasis of the legs. It occurred to me there was no

use in saving any fat in these flaps, so that I now make them almost entirely of skin. I cut off very carefully, with a sharp knife, all of the subcutaneous tissue (except at the very base of the flaps) and then replace the skin thus prepared upon the muscle, or whatever is left underneath.

I have noticed in making those flaps that, at the end of the operation, unless I have scarred the skin very carefully with a sharp knife, they turn very blue and it is almost impossible to make the sort of pressure which will keep them from suffering from the acute passive congestion, which is so fatal to these plastics. In other words, the flaps get plenty of arterial supply, but they do not get sufficient venous drainage. It would seem to me that in some cases I might well have made a whole thickness graft instead of attempting to secure some blood supply from the base of the flap itself. I have not yet used that method, but this work gives me the feeling that there is a good deal in this idea, and that it may be better, in planning flaps of a certain size, to use a whole thickness graft rather than to expect to be able to drain a very wide and thin flap.

DR ARTHUR M SHIPLEY (Baltimore) Last year, in Boston, I read a paper, and the two men who discussed it were totally at variance with my methods, but each was good enough to say that in spite of the fact that he did not approve of the methods which I had used, the statistics that I quoted spoke for themselves. I only arise, therefore, to say that in spite of the fact that many of us wonder why these flaps could not have been left attached, certainly the pictures presented speak for themselves and do not admit of very much criticism.

DR SUMNER L KOCH (Chicago) Doctor Farmer is to be congratulated on the very excellent results he has obtained in these cases and for his emphasis on one very important fact, namely, that it is the immediate treatment which the patient receives that counts for so much, for it is the man who first sees the patient who has the best opportunity for securing successful results such as Doctor Farmer has obtained.

I wonder if there are not a few other factors that ought to be emphasized in this connection. The amount of trauma that has been sustained by the flap is certainly a very important one. If the flap has been crushed and if it is white and devitalized, nothing in the way of good surgery can save it. If it is not crushed and if the tissue is still viable, then gentle and kindly treatment will help to make its preservation more certain.

I believe, and I say this without any critical intent, that the flap which was attached to the leg along its entire lateral margin would have survived completely if it had only been carefully cleansed and had been sutured back in place, and if pressure had been maintained over it to avoid congestion. I would not wish to cut such a flap away, for it appeared to have an adequate blood supply, and it should live if every form of trauma could be avoided. The lesson that Halsted and all of his pupils have taught us, that living tissue is fragile, delicate substance and that it will survive if it receives kindly treatment, is much to the point.

In the second place, I would not like to scrape the subcutaneous tissue from such a flap. Both Blair and Neuhof have shown that in the use of full thickness grafts success depends upon getting a graft of skin alone, without subcutaneous tissue attached, stretching the graft under normal tension with the aid of sutures, and maintaining smooth pressure over it to prevent congestion and to prevent oozing of blood and serum underneath the graft. The best way to secure a graft of skin alone is by sharp dissection. If we scrape it, we traumatize the capillaries and make more difficult the ingrowth into the

graft of the new capillaries upon which the life of the transplanted tissue depends

It seems to me Doctor Farmer's contribution is an important one and has a real place in that type of flap which is partially avulsed and which has only a distal attachment. Still I would not cut such a flap away, for even the distal attachment is of value. I would rather remove the subcutaneous fat from such a flap by sharp dissection, convert the flap into full thickness skin, and then lay it back in place and suture the free margin to the edges of the defect. Even the distal attachment would give some little blood supply that would help to safeguard the flap.

DR HENRY F. GRAHAM (Brooklyn) Doctor Koch has stolen most of my thunder, but I should like to say just a word. This is a valuable contribution if it is used with the experience of years behind it, but if it were broadcast that every avulsed flap should be cut off and scraped and sewed back in place again, irreparable damage would be done to many people.

This speaker's second case, especially the one where the leg flap was shown, was the one that especially aroused my interest, because I had a very similar case some years ago. A doctor while driving an automobile knocked down a child and brought him into the hospital with a very large and very dirty skin flap, similar to the one shown, if anything, I think, more extensive. The child was in shock at the time, and nothing could be done even in the way of cleansing. He was almost pulseless. He was given morphine, and as the best procedure that we could follow, as long as we could not take him to the operating room, we lifted up the flap, saturated the entire wound and the inside of the flap with Zonite, about 1:3 dilution, and put on wet compresses, so that the whole wound was soaked in it. The flap was laid back over the Zonite compresses and other wet compresses placed on the outside, it was then bandaged up and left. After four or five hours the shock diminished and it was possible to take the child to the operating room. The wound was cleansed and the entire free edge of the skin flap was carefully cut away, also the edge of the wound from which the flap had been removed, and the entire wound underneath was cleansed also, removing all the little particles of street dirt with scissors. The flap was sutured back in place, a dressing applied, and primary union was obtained in that wound without any infection at all.

When a viable flap is present this is a better procedure than to try this full thickness detached graft, but I know that there are many cases where skin has been cut away and where we could have used this full thickness graft method, and I shall certainly try it in the future.

DR A. W. FARMER (closing) We have thought of leaving avulsed skin flaps attached and making them into full free thickness grafts, and we have done it. The only case that we lost was one in which we did that. I do not know whether it has anything to do with pumping of arterial blood into the full thickness graft from the edge which is attached with inadequate drainage from it or not, but certainly I think, probably in my hands, it is better to detach the whole flap.

I would not agree with Doctor Koch. It is not a very nice thing for a surgeon to say carefulness is not necessary, but we have not found, with either the partial thickness or the full thickness variety of graft, that one needs to go to the degree of carefulness which would mean prolongation of the operation, *etc.*, where methods which are slightly more rough would make the operation more expeditiously performed.

We have not had any trouble with these free full thickness grafts, or other full thickness grafts done for other conditions in handling them fairly roughly.

PRESIDENT DALLAS B PHEMISTER'S VALEDICTORY*

BEFORE closing this annual meeting, I want to thank the fellows for the great effort which they have made toward making it a success. We have deviated in two respects from the usual procedure, in that the meeting was held at a resort, and also that there have been three full days devoted to the program. The attendance has been all that we could have hoped for. One hundred thirty-seven have registered and almost surely there are some who have not registered. The attendance at the meetings has been unusually good. There have been from 75 to more than 100 present during the active periods of all of the sessions.

It was feared that the amenities of the locale might divert a good many to the golf links, but despite the fact that it has rained to-day, I am inclined to give you credit for staying with us and especially making this last half day a success. You know how, usually, in the big cities, the audience is made up almost entirely of medical students on the last half day. On this occasion we have not any medical students to attend.

Of course you well understand that the success of the meeting has been a great personal satisfaction to me.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M D
1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English

Exchanges and Books for Review should be sent to James T. Pilcher, M D, Managing Editor, 121 Gates Avenue, Brooklyn, N Y

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa



THE OPERATIVE LENGTHENING OF THE TIBIA AND FIBULA*

A PRELIMINARY REPORT ON THE FURTHER DEVELOPMENT OF
THE PRINCIPLES AND TECHNIC

LEROY C ABBOTT, M D ,

AND

JOHN B DE C M SAUNDERS, M B , F R C S , (Edin)

SAN FRANCISCO, CALIF

FROM THE DIVISION OF SURGERY, DEPARTMENT OF ORTHOPEDIC SURGERY, UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL,
SAN FRANCISCO, CALIF

IN 1924, at the Shimer's Hospital for Crippled Children in St. Louis, we performed our first operation for lengthening the tibia and fibula in a patient in whom shortening of one leg had followed an attack of acute anterior poliomyelitis. In this patient, a gain in length of one and one-half inches was secured together with a decided functional improvement. Encouraged by this result, we decided to use the operation in a selected group of cases where shortening of one of the lower extremities constituted the major disability. A description of the procedure and the results obtained in the first six patients was published in January, 1927.¹

Further experience led to improvement in the technic of operation and to further development of apparatus and, by 1930, we had operated upon 73 patients, 48 of whom had lengthening of the tibia and fibula and 25 of whom had lengthening of the femur. The results obtained and the difficulties and complications encountered were discussed in further publications.^{2, 3, 4}

Our work stimulated an increasing interest in bone lengthening operations at various clinics in this country. The literature reflects this interest, since a substantial number of operations, with satisfactory results, have now been reported. Brockway,⁵ in reviewing a series of 46 leg lengthenings, states "When the operation for the lengthening of legs was first presented to the profession, it was believed by many to be a very formidable procedure involving considerable risk. Tested by actual experience, the operation has been found to be most practical and safe." Other surgeons have reported their results in a considerable group of cases. All of them, however, have recorded complications. While in some instances these complications might have been caused by inexperience with the details of the procedure, we know that these

* Read at the Annual Meeting of the American Academy of Orthopedic Surgeons, Los Angeles, Calif, January 20, 1938. Submitted for publication November 2, 1938.

This work was supported by the Florence Hellman Ehrman Donation for Orthopedic Children and the Christine Breon Fund for Medical Research.

complications will occur even in the hands of experienced surgeons who are thoroughly conversant with the operation. We can only attribute these complications to imperfections in the method which we have outlined in our previous publications.

These complications have led to a gradual loss of interest in the procedure of leg lengthening, and other less radical operations have been substituted. Shortening of the sound leg by fusion of the epiphyses at the knee, at the ankle, or both, has been developed in a highly scientific manner by Phemister.⁶ Resection of a segment of the femur or osteotomy of the femur with overlapping and fixation of the fragments by pins, has been practiced extensively by White.⁷ The excellent work of these surgeons has placed leg shortening on a sound basis. While leg shortening is not always free from complications, it is a much simpler undertaking than leg lengthening. It is our opinion, therefore, that, in the present stage of development of this operation, for the majority of patients with shortening of one of the lower extremities, the operation of leg shortening by the method of White or the epiphyseal arrest, as practiced by Phemister, is preferable to leg lengthening. There are certain patients, however, in whom epiphyseal arrest is no longer applicable because they have reached maturity. There are others of short stature in whom further reduction in height is undesirable and especially in patients with a marked degree of shortening, furthermore, it is to be borne in mind that leg shortening is carried out on the sound limb and on this ground may be objected to by the patient. Such indications for leg lengthening make it desirable to retain the procedure for a limited group and, in consequence, we have conducted further studies with a view to reducing the chances of complications. The results of these studies point to a clearer recognition of certain fundamental principles for the technic of operation. Our experience with the new technic has not been sufficiently extensive to merit any final conclusions, but we feel that our results should be recorded. This present communication is entirely in the nature of a preliminary report.

The Complications of Leg Lengthening—We believe a list of the common complications of leg lengthening is an essential preliminary to a discussion of methods.

- (I) Deformities of the foot (a) Valgus, (b) Equinus, (c) Equinovalgus, (d) Calcaneovalgus
- (II) Deformities of the knee (a) Genuvalgum, (b) Flexion contracture, (c) Relaxation of the knee
- (III) Anterior and medial bowing of the fragments of the tibia with mal- or nonunion
- (IV) Limitation of motion at the ankle
- (V) Weakening of the muscles of the leg
- (VI) Nerve complications (a) Paralysis or weakening of the muscles, (b) Disturbance of sensation
- (VII) Disturbance of circulation (chronic swelling of the leg)

(VIII) Infection (a) Infection of the operative wound, (b) Infection of pin wounds

(IX) Aseptic necrosis of bone (Compeire⁸)

The deformities of the foot, of the knee and the bowing of the fragments of the tibia, with consequent malalignment or nonunion, are caused by the failure of the soft parts to lengthen proportionately with the bones. The soft parts of major significance are the deep fascia, the intermuscular septa, the interosseous membrane and the periosteum. In addition, the tendinous content of the muscles offer great resistance to lengthening. For the most part, these fibrous structures are more intimately blended with the fibula than with the tibia, therefore, the segments of the fibula do not separate equally with those of the tibia.

At the ankle, the internal malleolus moves distally, while the external malleolus remains relatively fixed in position with not only subluxation at the lower tibiofibular joint but also alteration of the mortice of the ankle joint itself. The change in the mortice and the resistance of the peroneal muscles and of the ligaments passing from the external malleolus to the os calcis and astragalus, force the foot into valgus. This position may be converted into equinovalgus or calcaneovalgus, depending upon the relative resistance of the dorsal and plantar flexors of the foot.

On the lateral side of the knee, the deep fascia and the intermuscular septa blend intimately with the lateral ligaments and the capsule of the knee joint, the biceps femoris tendon and the iliotibial tract. The tension developed in these structures during the lengthening forces the knee into flexion and adduction. Stretching of the internal lateral ligament follows with resultant genuvalgum and instability of the joint. Occasionally the head of the fibula may separate from the tibia and move downward. This displacement has not been of great consequence yet it may stretch the external lateral ligament and cause further relaxation of the knee.

We believe limitation of motion at the ankle is caused by a traumatic arthritis which is due to the tremendous pressure on the articular surfaces of the joint. Where there is also malalignment of the joint, this arthritis may become progressive in character.

In our experience, injuries to the nerves, with partial paralysis of the muscles, disturbance of sensation and interference with circulation, have not been frequent or serious complications. These are undoubtedly the outcome of overstretch during lengthening.

In a procedure of such magnitude, which requires wide opening of the medullary canal, infection of the operative wound may readily occur unless the strictest attention is paid to asepsis and to the gentleness with which the tissues are handled. Pressure necrosis of the skin and soft tissues, with attendant osteomyelitis, is due to the lack of complete control of the fragments. Infection of the pin wounds is caused by trauma during their insertion, by pressure necrosis of the soft tissues and bone and also by too frequent changes of dressings. It is our experience that the dressings should not be changed unless there is absolute necessity for it. An unrecognized, but none the less

important, factor in the production of osteomyelitis is the migration of pins from side to side. Undue irritation from faulty metal used in the construction of the pins is another important cause of bone destruction. We agree with the conclusions of Compere,⁸ in that aseptic necrosis of the fragments may result from too extensive stripping of the periosteum. In the presence of infection, this aseptic necrosis may change to septic necrosis, and resultant osteomyelitis with all its disastrous sequelae.

The weakness of the muscles, apart from nerve injury, may be attributed to overstretching of their fibers beyond the limits of their elasticity.

Discussion of the Principles of Leg Lengthening—In early publications, we stressed the importance of the application of certain fundamental principles in order to lengthen a bone, which were: First, traction must be made directly on the bone itself, second, in order to overcome the elastic resistance of the soft parts, traction must be slow and continuous in type, and third, to avoid harmful pressure on these soft parts, alignment and contact of the fragments must be maintained during the lengthening process. Further experience with the procedure has convinced us that with the operation, as performed even with the four-pin control, the application of the third principle is difficult of attainment. We early recognized that an important cause of malalignment was the resistance of the fibrous structures, particularly those attached to the fibula. We, therefore, advised and carried out increasingly radical divisions of the deep fascia, the intermuscular septa, the periosteum and the interosseous membrane. A just criticism was offered by Haboush and Finkelstein,⁹ on the ground that the division of these structures was at an incorrect level. We had already realized this at the time and further studies emphasized it.

In the course of our studies we carried out many anatomic dissections of the leg. Our purpose was: First, to determine the exact anatomic relation of the deep fascial envelope, the intermuscular septa and the interosseous membrane to the tibia and fibula. Second, we wished to satisfy ourselves as to the exact relation of the muscles of the leg to these fibrous structures and to the bone. These dissections disclosed that no matter how radical the division of the fascial envelope, the intermuscular septa, the interosseous membrane and the periosteum, considerable resistance was still offered to lengthening. This resistance was due to the enormous fibrous content of the muscle bellies. A fact not fully appreciated, is that in any muscle the fleshy part contains an amount of fibrous tissue equal to the bulk of its tendon. The tendon of a muscle passes from its origin to its insertion, being only expanded in its muscular substance. Because of this arrangement, complete division of the fibrous parts, *etc.*, leaves a large part of the resistant fibrous elements untouched. When a muscle is stretched beyond its inherent elasticity it can only yield at the expense of its passive elements. Destruction and breaking down of these elements leads to permanent damage with scar formation in the muscle substance. We regard the loss of muscular power as due, not only to overstretch, but also to contractures in the muscles. This is evidenced by the progressive development of fixed deformity, not infrequently met with in leg lengthening.

It is evident, therefore, that the prevention of overstretch of the muscles demands either lengthening of their tendons at the ankle or the freeing of their origins from the upper parts of the tibia and fibula. Multiple tendon lengthening is impractical and would produce a widespread weakness of the muscles which would defeat our purpose. The only alternative, therefore, was to consider the practicability of freeing the origin of the muscles sufficiently to permit the performance of such osteotomies as would allow bodily migrations of these muscles with the descending fragments of the bones. To determine whether or not this plan was feasible, we carried out anatomic dissections.

Anatomic Considerations—In these dissections we were primarily concerned with the following structures: (A) The deep fascia, (B) The interosseous membrane, (C) The origin of the muscles, (D) The points of fixation of the blood vessels and the nerves, (E) The nutrient vessels.

(A) *The Deep Fascia*—This forms a complete envelope for the leg except over the subcutaneous surface of the tibia and over a small triangular area about the lateral malleolus of the fibula. In these regions it is continuous with the periosteum of these two bones. Proximally, it blends with the fascia lata and is strengthened by expansions from the tendons about the knee. The fascia is notably dense over the anterolateral aspect of the leg where its deep surface gives partial origin to the extensor and peroneal musculature. Distally, it presents additional fibers which constitute the series of retinacula which bind the tendons in the region of the ankle and the foot.

On the anterolateral aspect of the leg two intermuscular septa, the anterior and posterior peroneal septa, pass from the deep fascia to the fibula. The anterior peroneal septum encloses the superficial peroneal nerve and separates the extensor from the peroneal muscles. The posterior peroneal septum separates the peroneal muscles from the muscles of the calf. These septa are expanded and especially thick where they blend with the deep fascia and they divide the leg into three osteofascial compartments—an anterior, a lateral and a posterior or flexor compartment. There are several other subsidiary septa. One of these extends from the posterior peroneal septum across the posterior compartment of the leg on the surface of the deep flexor muscles to meet the tibia. It encloses the posterior tibial vessels and nerves and is best defined in the distal two-thirds of the leg. Another fairly strong sheet of fascia covers the tibialis posterior muscle and separates it from the flexors of the toes. This fascial septum is continuous with the fascia on the surface of the popliteus muscle where it is strengthened by an expansion from the tendon of the semimembranosus. In the anterior compartment there are a series of weak and ill defined septa separating the individual extensor muscles.

(B) *The Interosseous Membrane*—The interosseous membrane occupies the interval between the two bones. Above, it has a large aperture for passage of the anterior tibial vessels, below, a similar one for the passage of the perforating peroneal artery. Posteriorly, it gives partial origin to the tibialis posterior muscle while, anteriorly, it is directly related, in the proximal two-thirds of the leg, to the anterior tibial vessels.

(C) *The Origin of the Muscles*—The origins of the muscles are given in the following tabulated form (Table I)

TABLE I

MUSCLES OF THE ANTERIOR COMPARTMENT

<i>Tibialis Anterior</i>	<i>Extensor Digitorum Longus</i>	<i>Extensor Hallucis</i>
Lateral condyle tibia	Proximal two-thirds anterior	Intermediate two-thirds an-
Proximal two-thirds lateral	half of medial surface of	terior half of medial sur-
surface of tibia	fibula	face of fibula
Interosseous membrane	Interosseous membrane	Interosseous membrane
Overlying deep fascia	Neighboring septa	Neighboring septa
Septum between it and ex-	Overlying fascia	
tensor digitorum longus		
	<i>Peroneus Tertius</i>	
	Distal one-third of the an-	
	terior half of the medial	
	surface of fibula	
	Interosseous membrane	
	Neighboring septa	

MUSCLES OF THE LATERAL COMPARTMENT

<i>Peroneus Longus</i>	<i>Peroneus Brevis</i>
Head and proximal two-	Distal two-thirds of the
thirds of the lateral sur-	lateral surface of fibula
face of fibula	Intermuscular septa
Intermuscular septa	
Overlying fascia	

MUSCLES OF THE POSTERIOR COMPARTMENT

<i>Gastrocnemius</i>	<i>Soleus</i>
Lateral head	Head and proximal one-
Distal part of lateral epi-	third of posterior surface
condylar line of femur and	of fibula
lateral surface of condyle	Fibrous arch over popliteal
Medial head	vessels
Medial side of popliteal sur-	Oblique popliteal line
face of femur	Intermediate one-third of
	medial border of tibia

DEEP GROUP

<i>Popliteus (insertion)</i>	<i>Flexor Digitorum Longus</i>	<i>Flexor Hallucis Longus</i>
Popliteal line and triangular	Intermediate three-fifths	Distal two-thirds posterior
surface above it	posterior surface of tibia,	surface of fibula
	medial to vertical line	Fascia over tibialis poste-
	Fascia on surface of tibialis	rior
	posterior	Interosseous membrane
		Posterior intermuscular
		septum

<i>Tibialis Posterior</i>
Posterior half of the medial
surface of fibula
Proximal two-thirds of the
posterior surface of tibia,
lateral to vertical line
Lateral condyle
Interosseous membrane
Fascia covering it

LENGTHENING OF TIBIA AND FIBULA

(D) *Points of Fixation of the Vessels and Nerves*—The vessels and nerves of the leg present very definite points of fixation. The common peroneal nerve passes from under cover of the tendon of the biceps femoris muscle to

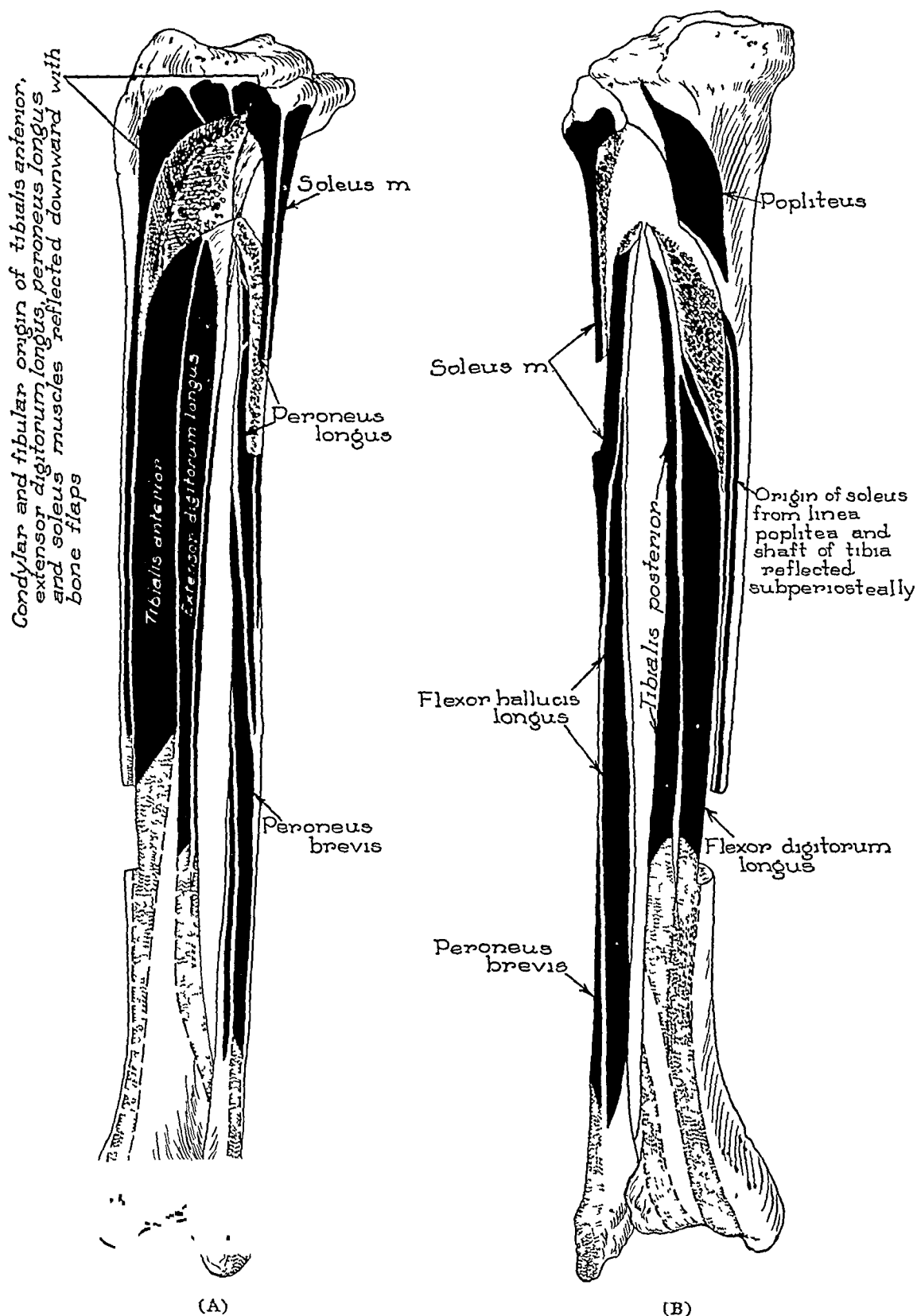


FIG 1 (A and B) —The origin of the muscles from the anterior and posterior surfaces of the tibia and fibula with osteotomies of both bones in the anteroposterior plane to permit bodily migration of the origin of the muscles with the descending fragments

pierce the fascial envelope of the leg. It winds around the neck of the fibula and into the lateral compartment in front of the posterior peroneal septum. Just prior to piercing the fascial envelope, it is held in place by a fibrous expansion from the tendon of the biceps. The popliteal vessels are fixed at two points. The first point of fixation is where its anterior tibial division passes through the interosseous membrane, the second is where the posterior tibial artery passes beneath the arch of the soleus.

(E) *Nutrient Vessels*—The nutrient artery to the tibia is usually given off from the posterior tibial artery just below the fibrous arch of the soleus. It passes medially and downward under cover of the soleus to pierce the substance of the flexor digitorum longus and enters the bone. This vessel gives off several muscular branches, one of which is found entering the soleus muscle at about the level of the oblique popliteal line. The nutrient artery to the fibula is a branch of the peroneal artery. It may enter the bone at the junction of its upper and middle thirds or at its lower and middle thirds.

The anatomic arrangement may be summarized by recognizing that the muscles passing from the tibia and fibula to the foot arise from a bony and fibrous Gothic arch with lateral pillars consisting of the shafts of the two bones (Fig. 1 a and b). The outer fibular pillar is completely invested with muscles and its surfaces for attachment are extended by the intermuscular septa. The inner tibial pillar gives origin to muscles except for its medial subcutaneous surface. The interval between the pillars is occupied by the interosseous membrane which affords additional surfaces for the origin of muscles. The deep fascia invests the leg circumferentially with the exception of the medial surface of the tibia. In the region of the apex of the arch it gives origin to the muscles on the anterolateral aspect of the leg.

With this arrangement in mind, we considered a procedure for freeing these muscles by a complete subperiosteal reflection from the upper parts of the tibia and fibula. The magnitude of the periosteal reflection necessary to accomplish this would deprive large segments of both bones of a large part of their blood supply. In addition, this procedure, necessarily blind, would endanger the important blood vessels and nerves in the vicinity. This method was, therefore, not adopted and, later, we decided that these important structures could be better exposed by two incisions, one, on the anterolateral and the other on the posteromedial aspects of the lower thigh and upper leg.

The following cases illustrate the practical application of these new principles. All of these operations were performed with a tourniquet applied.

Case 1—E. G., male, age 13. Admitted, March 10, 1936.

Chief Complaint—Shortening of the right leg.

Present Illness—Acute anterior poliomyelitis at the age of six, with residual paralysis of the right leg.

Physical Examination—Marked atrophy of the muscles of the right leg. The muscles which showed moderate power were the gastrocnemius, the peroneus longus and brevis. The foot was in equinovalgus. There were two inches of shortening.

Operation, March 19, 1936—The operation was performed as a single stage procedure. The upper attachment of the muscles, the popliteal and tibial vessels, and the

peroneal and tibial nerves were exposed through anterolateral and posteromedial incisions. The origin of the peroneus longus, the soleus, the extensor digitorum longus and the tibialis anterior muscles were freed subperiosteally from the upper ends of the tibia and fibula in the region of the arch formed by these two bones. The intermuscular septa, the interosseous membrane and the deep fascia were divided. The fibula was osteotomized by an oblique section of its upper end. The tibia was divided by a transverse cut through the posterior cortex just below the level of the linea poplitea. The extremities of this division were joined by linear sections of the cortex, three inches in length, on the middle of the medial and lateral surfaces of the tibia. The four-pin apparatus was applied and the osteotomy was completed by a cross-cut of the anterior crest of this bone, uniting the linear sections on either side.

Postoperative Notes—An infection developed about the upper pins, from which a quantity of pus discharged for several days. The temperature subsided gradually and the wound closed. Despite the infection, lengthening was continued and the desired two inches was obtained.

Final Result—Union with satisfactory alignment, two inches gain in length and excellent improvement in function. The slight equinus deformity present before lengthening was subsequently corrected by stabilization of the foot.

COMMENT—The lessons we learned from our experience with this patient were that the operation was entirely too extensive for one stage, and that the periosteal stripping was excessive. These difficulties were no doubt related to the infection of the pin wounds and the development of a mild localized osteomyelitis.

In our next case, we decided to perform the operation in two stages, and we also planned an osteotomy of the tibia which would reduce the amount of periosteal stripping.

Case 2—B. W., female, age 13. Admitted, November 10, 1936.

Chief Complaint—Shortening of the right leg.

History—At the age of 13 months, this patient had acute anterior poliomyelitis, which was followed by paralysis of the right leg. At the age of 10, she had a stabilization of the right foot.

Physical Examination—There was no power demonstrable in the muscles on the posterior aspect of the leg. The dorsal flexors of the foot and the extensors of the toes were strong. There were two and one-half inches of shortening of the right lower extremity, two inches of which were confined to the leg.

Operation, November 13, 1936—As in Case 1, the muscular attachments, the vessels and bones were exposed through two incisions. The muscles were detached in essentially the same manner as in Case 1 except that the periosteal stripping was less extensive on the posterior aspect of the tibia. The fascia, the intermuscular septa and the interosseous membrane were freely incised and the fibula was obliquely transected at its upper end. The beginning of an oblique osteotomy, which was contemplated for the second stage, was commenced on the posterior aspect of the tibia at the lower end of the linea poplitea. From this site it was continued forward and downward for approximately one inch.

Second Stage Operation—November 25, 1936. The four-pin apparatus was applied. The posteromedial incision of the first stage was continued forward and downward onto the crest of the tibia. The periosteum was stripped from the anterior half of the tibia for a distance of three inches and the oblique osteotomy of this bone was completed. A half inch of lengthening was obtained.

Postoperative Notes—Lengthening was begun December 2, 1936, seven days after the completion of the second stage. By December 13, lengthening was increased two

inches, which means that one and one-half inches had been gained in 11 days. It was noted that the fragments of the tibia tilted forward, and that this was reduced by flexion of the knee. There was some persistence, however, of this tilting which prevented contact of the two fragments distally.

Final Result—At the present time, one year and 10 months after operation, union of the fragments has taken place only at their upper halves.

COMMENT—The inferior extremity of the upper fragment failed to unite solidly to the lower fragment because of the separation of the fragments and of the extensive stripping of the periosteum from the lower end of the upper fragment.

The patient is now walking with a caliper brace and she has good function. There have been no complications of knee or foot, no internal bowing of

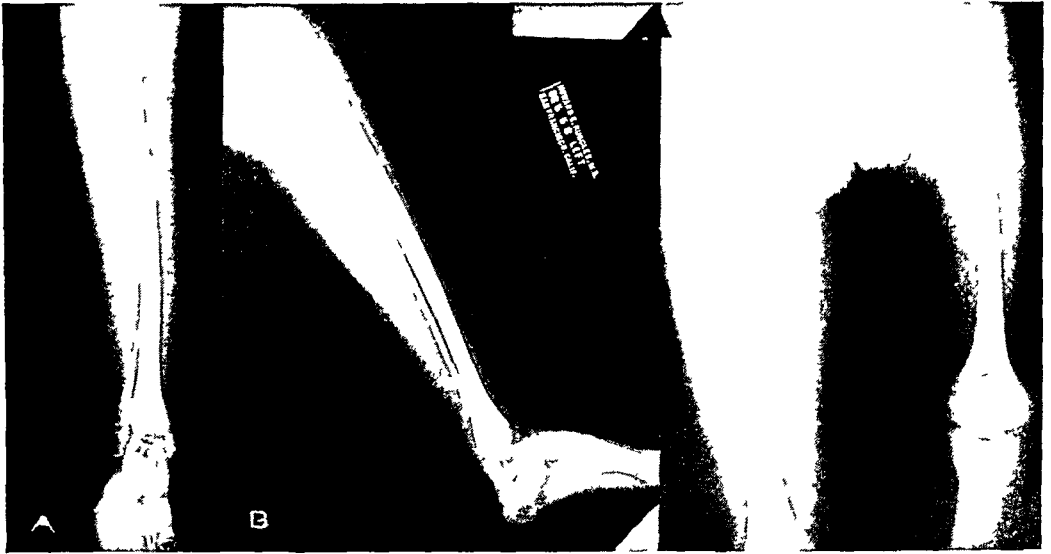


FIG 2 (A, B, and C)—Case 3. Two and one-half inches of shortening of the tibia and fibula and four inches of shortening of the femur. Total shortening of six and one-half inches. Note closure of lower femoral and upper tibial epiphyseal lines with compensatory bowing of the fibula. Calcaneus deformity of the foot.

the tibia and no indication of injury to the blood vessels or nerves. A tendon transplant on the foot together with a minor bone grafting operation will free this patient from apparatus.

Case 3—W. M., male, age 13. Admitted, September 13, 1936. Referred by Dr. Harold H. Hitchcock, of Oakland.

Chief Complaint—Progressive shortening of the left leg over a period of 11 years.

History—At the age of two, the patient had tuberculosis of the left hip. He was treated conservatively until the age of nine, when an arthrodesis of the hip was performed. Following this, he sustained two fractures of the left tibia in the region of the knee, and he was supposed to have had an attack of acute anterior poliomyelitis affecting the left leg, time of onset unknown.

Physical Examination—The patient walks with crutches. His left hip is fixed in 40° of flexion, neutral as regards abduction, adduction and rotation. There is a marked atrophy of the bones and muscles of this extremity and there is a calcaneus deformity of the foot. The measurements showed six and one-half inches of actual shortening of the left lower extremity, four inches in the thigh and two and one-half inches in the leg. The roentgenograms showed incomplete fusion of the left hip, marked shortening

LENGTHENING OF TIBIA AND FIBULA

of the extremity and obliteration of the lower femoral and upper tibial epiphyseal lines. There was a marked internal bowing of the tibia and a compensatory bowing of the fibula so that its middle portion was displaced behind the tibia (Fig 2 a, b and c).

Operations, December 15, and December 22, 1936—These were carried out in two stages. In the first stage, the approach used was the same as that employed in Case 2. At this time the fibula was sectioned obliquely together with freeing of the fibrous structures. At the second stage, the four-pin apparatus was applied and the tibia was osteotomized in a Z-shaped manner, as in Case 1, through an extension of the posteromedial incision. A half-inch gain was obtained.

Postoperative Notes—Lengthening was carried out for three weeks after completion of the second stage, when an increasing equinus rendered subcutaneous tenotomy of the tendo achillis necessary. Lengthening was then continued and, at the end of 48 days, three inches had been gained. There was good alignment and considerable formation of callus (Fig 3 a and b).

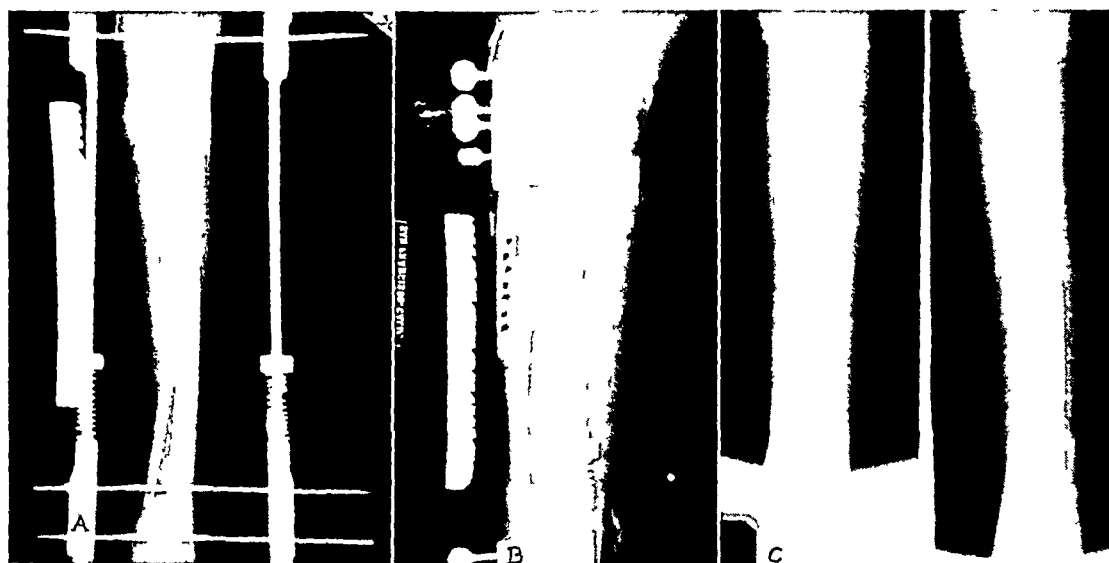


FIG 3 (A and B)—Case 3. Anteroposterior and lateral views 48 days postoperative showing three inches gain in length with good alignment and beginning formation of callus. (C)—Seven months after operation with restoration of the medullary canal of the tibia.

Subsequent Course—April 17, 1937 (Approximately seven months after operation). Roentgenograms show satisfactory length and alignment with union and restoration of the medullary canal (Fig 3 c).

May 4, 1937—The patient was readmitted. He is now 14 years of age. On this day, he slipped and fell, fracturing the femur at the upper margin of the plaster encasement which he was wearing for the protection of his osteotomized tibia and fibula.

Physical Examination—There was considerable swelling, ecchymosis and crepitus at the site of fracture. Roentgenograms disclosed an irregular, transverse fracture at the middle third of the left femur. The following plan of treatment was carried out.

May 5, 1937—A Hoke traction spica was applied with a special leg lengthening apparatus incorporated.

May 12, 1937—Through an oblique incision, the tendons of the rectus and vastus intermedius muscles were freed down to their insertions at the patella. The rectus tendon was sectioned just above the patella and turned upward. The vastus lateralis and medialis were freed from the lateral aspects of the patella and from the intermedius tendon. The intermedius muscle was then sectioned at the junction of its tendon and belly. Tenotomy of the tendon adductor magnus at the level of the adductor tubercle and freeing of the tendon to the level of the lower part of Hunter's canal liberated the origin of the lower part of the vastus medialis. The rectus and intermedius tendons were sutured to each

other with plenty of slack. The insertions of the vastus lateralis and medialis were moved upward and sutured to the lateral margins of the intermedius and rectus tendons. The site of the fracture was exposed and the periosteum stripped from the ends of the upper and lower fragments.

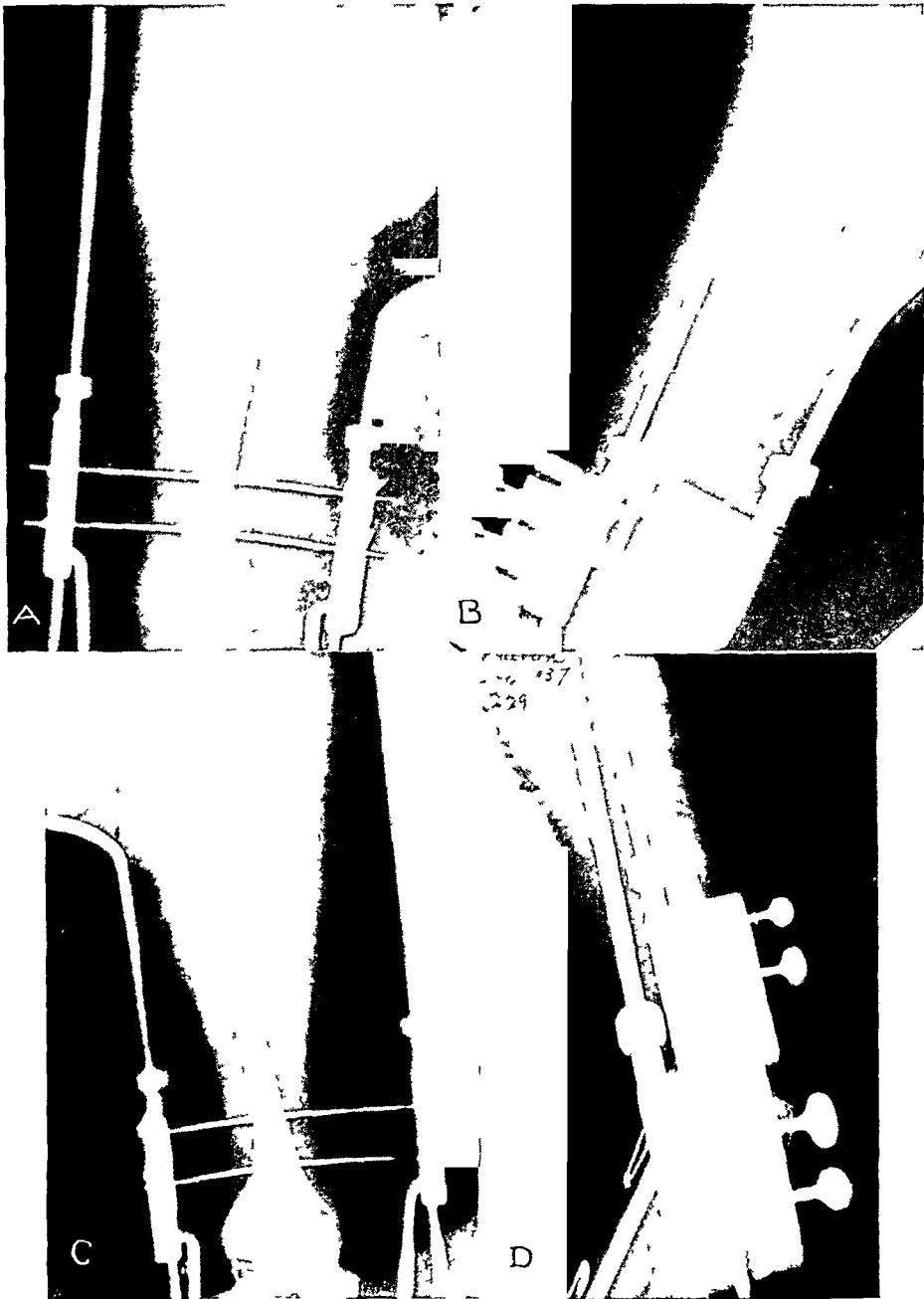


FIG. 4 (A and B)—Case 3. Anteroposterior and lateral views 14 days after fracture of the femur with apparatus applied for lengthening. (C and D)—Anteroposterior and lateral views, 20 days after fracture. Note extensive formation of callus.

May 18, 1937—Under general anesthesia, two, one-eighth inch pins were passed horizontally through the lower end of the femur, tension was applied and one-half inch gain secured. Roentgenograms show traces of formation of callus (Fig. 4 a and b).

May 24, 1937—Roentgenograms taken 20 days after fracture, and 12 days after operation, show increased formation of callus at the site of fracture (Fig. 4 c and d).

LENGTHENING OF TIBIA AND FIBULA

May 26, 1937—Two oblique pins were drilled through the cortices of the upper fragment, the projecting ends of which were fastened to the lateral bars of the traction apparatus. This was done because the patient was rotating in his spica and there was insufficient counter traction.

June 10, 1937—Roentgenograms showed massive formation of callus and two inches of lengthening.

July 19, 1937—Two and one-third inches of lengthening.

September 30, 1937—Additional formation of callus and an increase in the size of the shaft of the femur (Fig 5 a and b). Total gain in length was five and one-third inches (Fig 5 c). At this time the patient had two inches of shortening.

Final Result—September 20, 1938. Due to the patient's having grown two inches during the past year, the measurements now show nearly three inches of shortening. We



FIG 5 (A and B)—Case 3. Anteroposterior and lateral views five months after fracture showing extensive formation of callus with union. Gain in length of two and one-third inches. Total gain in length of extremity, five and one-third inches. (C)—Anteroposterior view eight months after fracture. Note correction of alignment by formation of callus on the outer aspect of the lower end of the upper fragment.

made a mistake of not effecting an arrestment of the lower femoral and upper tibial epiphyses of the normal side. A plaster of paris encasement has been worn since the last operation, which is now being changed to a brace.

COMMENT—Our experience in this case raises a number of important points relative to formation of callus. This patient had six and one-half inches of shortening which increased to eight and one-half inches through further growth. By operative lengthening of the tibia, fibula and femur, five and one-third inches were gained. The formation of callus in the femur was unusually massive, and the question arises as to whether or not this might be the outcome of procedures carried out during a critical period of new formation of bone. It is interesting to observe that there was an interval of seven days between the injury and operation, and a further period of six days between the operation and the commencement of lengthening. We have asked ourselves the question, whether or not the trauma incident to the operation increased the production of callus at a stage when preosseous tissue was being formed, and furthermore, did the stimulation provided by traction incite a more rapid

and extensive proliferation in an already active osteogenic tissue? The roentgenologic evidence was sufficiently suggestive to warrant, in a case of lengthening presented later in this communication, utilization of this possible critical period in bone formation

In the following cases a new apparatus was employed, the principles of which were suggested by one of our associates, Dr Francis E West

Description of Apparatus—This consists of the following parts (Fig 6 a and b)

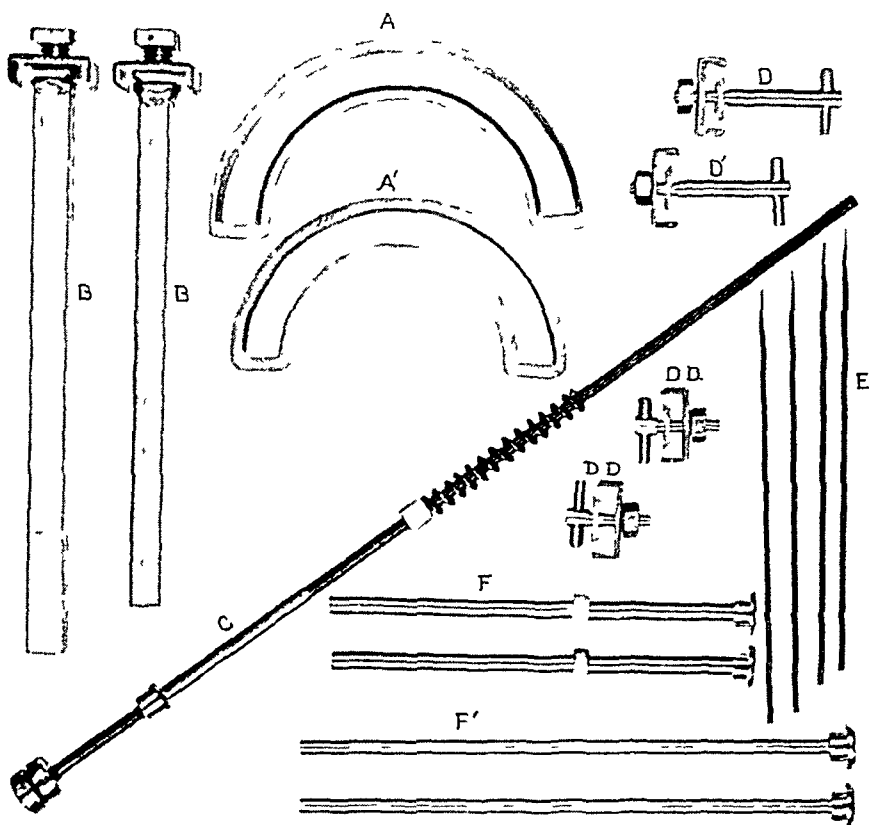


FIG 6(a)—Oblique pin apparatus (A) Half hoops with curvilinear notches, (B) Hollow telescoping segments, (C) Threaded traction bar with nut and recoil spring (D) Clamps with adjustable cylinders for pins, (E) Stainless steel drill pins, (F) Telescoping cylinders for support of control pins

(A) Two half-hoops with curvilinear slots

(B) Two hollow telescoping segments, each seven inches in length, equal in cross-section, inner segment being one-half inch wide and the outer nine-sixteenths of an inch wide

(C) Four clamps with adjustable rotating cylinders to hold the traction pins

(D) A threaded traction bar, 15 inches in length, one-quarter of an inch in diameter, with a recoil spring, three inches long

(E) Four stainless steel drill pins, six inches long and one-eighth of an inch in diameter

(F) Two telescoping cylinders for control pins

In assembling the apparatus, the hollow segments are telescoped over each other. The threaded traction bar with the recoiled spring is passed down their centers and the ends are fixed to the two half-hoops by nuts and screws. The four adjustable clamps are now attached to the two half-hoops, two are placed so that their metal cylinders lie above and below the metal hoops, the other two with their cylinders lie on the medial surfaces of the hoops.

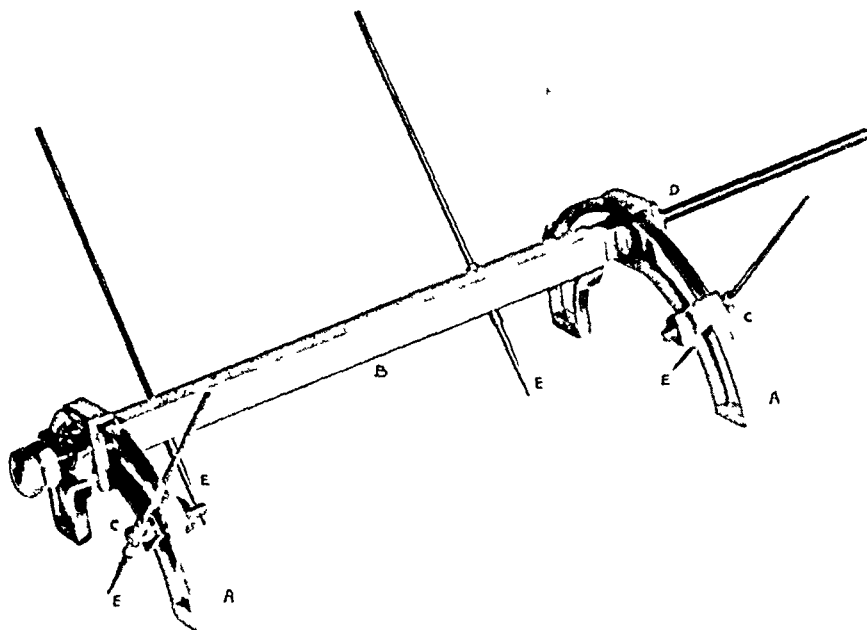


FIG 6(b) —Oblique pin apparatus, assembled (A) Half hoops with curvilinear notches, (B) Rectangular telescoping segments, (C) Adjustable pin clamps, (D) Threaded bar with nut and recoil spring, (E) Four stainless steel pins

During the application, the apparatus is held over the anterior surface of the leg by an assistant. The four clamps with rotating cylinders are moved along the curvilinear notches in the half-hoops until the cylinders point in an oblique direction towards the middle of the lateral and medial surfaces of the upper and lower ends of the tibia. The pins are then passed through the cylinders and turned through the corresponding cortices of the shaft of this bone. All four pins also pass through the posterior cortex of the tibia. With the pins engaged, the clamps holding the cylinders are fixed to the curvilinear notches in the half-hoops.

To secure further control of the fragments we have included in our illustration telescoping cylinders which may be attached to the outer segments of the upper and lower hoops on both sides of the leg. To these cylinders, adjustable pins may be attached with their central ends set against the lateral

surfaces of the terminal portions of the upper and lower fragments of the tibia. In Cases 4 and 5, with osteotomy of the tibia in the transverse plane, we employed a single control pin set against the anterior surface of the lower end of the upper fragment. We have not used control pins with the osteotomy of the tibia performed in the anteroposterior plane.

Case 4—L. B., male, age 16. Admitted, March 3, 1937.

Chief Complaint—Shortening of the right leg and deformity of the foot.

History—Acute anterior poliomyelitis in 1931, with residual paralysis affecting the right leg. His former treatment consisted of braces and physical therapy.

Physical Examination—There was atrophy of the right lower extremity with a moderate amount of power in the soleus, gastrocnemius and the extensor hallucis longus. The foot was held in a position of valgus. There were two and one-quarter inches of shortening with two inches confined to the tibia and fibula.

First Stage Operation—March 10, 1937. Through an anterolateral incision, the common peroneal nerve, popliteal and anterior tibial vessels were exposed. The fibula was sectioned obliquely. The posterior cortex of the tibia was sectioned transversely just below the lower end of the linea poplitea. At the outer extremity of this osteotomy a linear division was made at the cortex at the middle of the lateral surface of the tibia extending downward a distance of about three and one-half inches. A plaster encasement was applied for support.

Second Stage Operation—March 22, 1937. On reopening the lower portion of the operative wound, we discovered that there had been almost complete union of the soft part structures and fibula. These tissues had to be separated a second time. The oblique pins were inserted into the upper and lower ends of the tibia and the traction apparatus was applied. With a power-saw, the osteotomy was completed by dividing the cortex of the medial surface of the tibia paralleling the cut made through the outer cortex of this bone at the first operation. These linear cuts were joined below by a transverse division of the crest of the tibia. A fifth pin was attached to the rectangular piece of the traction bar and fitted against the anterior aspect of the cortex of the upper fragment. The tendo achillis was not lengthened.

Postoperative Notes—Lengthening in this patient was gradually secured with the knee held in the flexed position. A gain of one and three-quarter inches was recorded, with good alignment. There was slight anterior tilting of the lower end of the upper fragment which was controlled by the fifth pin. After the desired length was secured, extension of the knee was completed in 10 days. The apparatus was removed 58 days after lengthening was begun, and a plaster encasement was applied for immobilization.

May 30, 1937—A walking plaster encasement was applied. The patient had full length, with union in excellent alignment, and there was a marked improvement in function. The deformity of the foot was corrected, subsequent to the lengthening, by stabilization.

Case 5—T. F., male, age 15. Admitted, March 7, 1937.

Chief Complaint—Shortening of the right leg.

History—Anterior poliomyelitis at the age of three, with involvement of all four extremities. There had been complete return in function except in the right lower extremity.

Physical Examination—There was a marked shortening, complete paralysis of this extremity and valgus deformity of the foot. The shortening amounted to two and one-quarter inches, which was confined to the leg.

Operation—March 9, 1937. The operation was performed in two stages in exactly the same manner as in Case 4. Again, there was a tendency for the lower end of the upper fragment to tilt forward and a fifth pin was used for control. Alignment was then easily maintained. A gain of two inches was secured. There were no important com-

plications other than a slight sloughing at the entrance of the control pin, which cleared up rapidly after the pin was removed. The apparatus was taken off in two months.

Postoperative Notes—June 15, 1937. The patient was wearing a walking plaster splint for protection. Roentgenograms showed union, with good alignment, and a gain of two inches in length.

September 1, 1938.—There was union with good alignment. Function was markedly improved.

In Cases 4 and 5, there was a moderate anterior tilting of the lower end of the upper fragment of the tibia. This was controlled in part by flexion of the knee, but complete contact of the fragments could only be maintained by the use of a fifth pin. We must take into account, however, that the tendo achillis was not lengthened in either of these cases and was undoubtedly the cause of the forward tilting of the lower end of the upper fragment.

Further dissections have shown that the malalignment of the tibial fragments in the anteroposterior plane is caused by the tension thrown upon the intact gastrocnemius muscle. The soleus muscle plays no part in the production of this deformity because its origin has been released. Lengthening of the tendo achillis is not sufficient to relax the gastrocnemius. We have found the logical method to be the division of the tendon of the gastrocnemius where it joins the tendon of the soleus. The gastrocnemius muscle is then rendered slack by the transplantation upward of its tendinous portion to the fascial surface on the posterior aspect of the soleus. We have fixed this tendinous portion of the gastrocnemius in its new position by silk sutures and have reinforced the junction by using the tendon of the plantaris as a living suture.

Another lesson learned from our experience with Cases 4 and 5, is that the interval separating the two stages of operation should not be longer than five or six days. If this period is exceeded, the tissues become firmly reattached and require a second separation.

In the next patient we tried to reproduce the same conditions for the formation of bone as were present in Case 3. These did not exactly coincide, however, because we did not strip the periosteum during the second stage of the procedure. In analyzing the problem we planned a supplemental bone-grafting operation in case there was not sufficient formation of callus.

Case 6—M. D., female, age 18. Admitted, October 17, 1937.

Chief Complaint—Shortening of the left lower extremity.

History—Acute anterior poliomyelitis at age two, with residual paralysis in the trunk, upper and lower extremities. She had conservative treatment until 10 years of age, when the left foot was stabilized. In 1933, the tendo achillis was lengthened on the left side. In 1935, she had corrective jackets and a fusion operation upon her spine. At present, she complains of lack of balance due to shortening of the left lower extremity. The balance and gait were improved by a lift on the left shoe.

Physical Examination—There was extensive involvement of the muscles of all four extremities and the trunk. She walked with a bilateral gluteus medius gait. She had difficulty in maintaining balance without a lift of one and one-half inches on the left shoe. The gait was improved by walking on boards of the same height. There was two inches of shortening, one and one-quarter inches being present in the leg.

First Stage Operation—October 20, 1937. Under general anesthesia, an oblique inci-

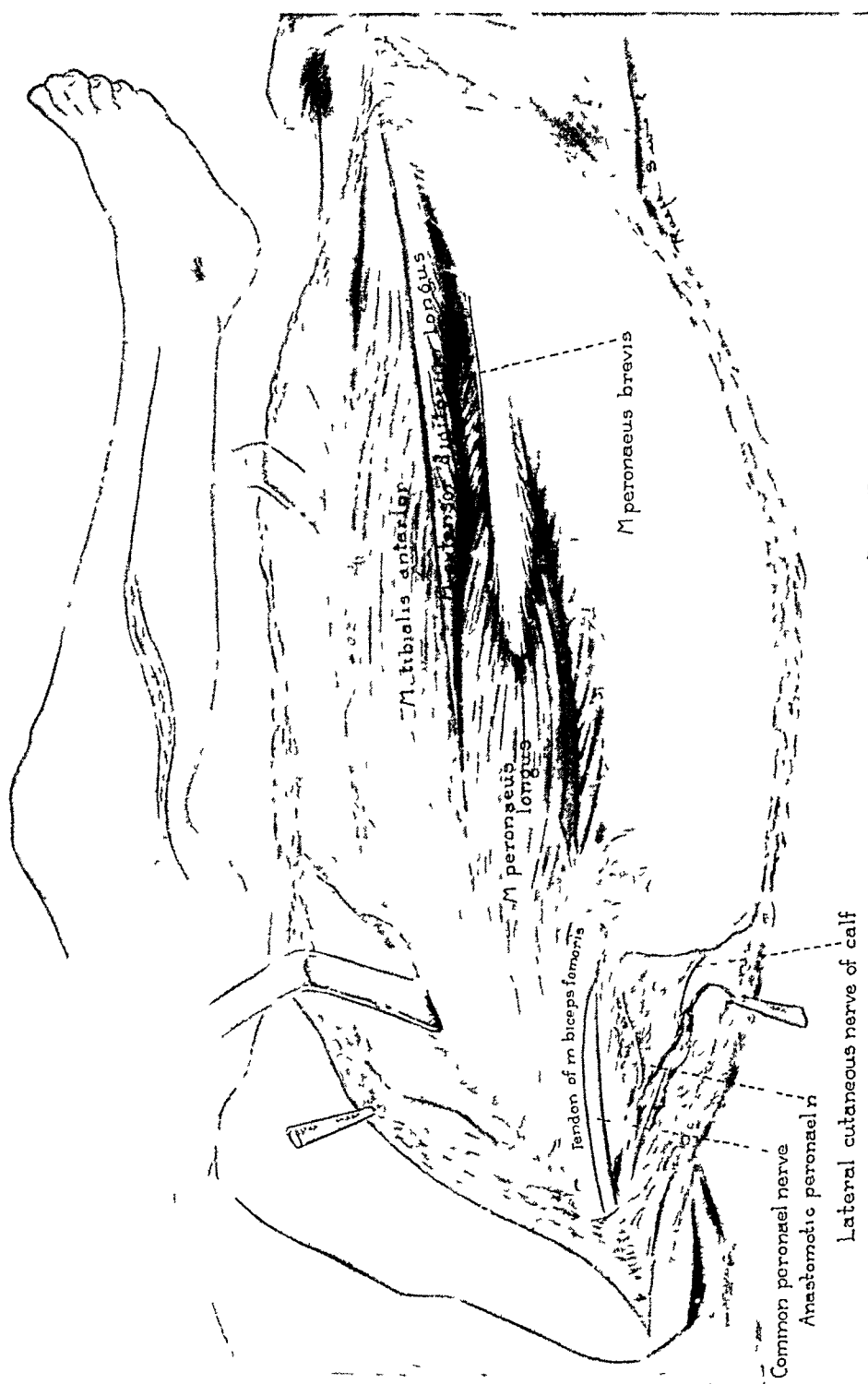


FIG 7(a) —First stage. Insert shows incision. Illustration shows origin of muscles and relation of common peroneal nerve to biceps

sion was made through the skin and periosteum on the anterior surface of the left tibia at the junction of the upper and middle thirds. The periosteum was stripped from the crest and the adjacent bone. An oblique osteotomy, two inches in length, was performed with drill and osteotome. A plaster encasement was applied.

Second Stage Operation—October 26, 1937. A vertical incision was made on the posterior surface of the leg extending from the lower margin of the popliteal space to the junction of its lower and middle thirds. After retraction of the lesser saphenous vein, the common peroneal and cutaneous nerves, the two heads of the gastrocnemius were separated from each other down to their union with the tendinous portion of the soleus. With the neurovascular bundle freed and retracted posteriorly, the origins of the soleus and the tibialis posterior were reflected subperiosteally from the posterior aspect of the tibia and fibula and the fibrous arch between these two bones. An oblique osteotomy was performed through the neck and upper portion of the fibula. The popliteus muscle was turned upward and an osteoperiosteal graft, two inches in length, was cut from the posterior surface of the upper fragment just above the osteotomy. With lengthening, this graft would bridge the osteotomy. The tendinous insertion of the gastrocnemius was transplanted upward a distance of two inches to the posterior aspect of the soleus.

November 4, 1937—Under general anesthesia, the oblique pin apparatus was applied. The upper pins were placed in the tibia while the lower pin was passed through the fibula and tibia. A Mathews wire was then inserted in the os calcis. The leg was supported on an adjustable splint with the knee held in 45° of flexion. With the lengthening, traction was also applied to the pin through the os calcis.

November 9, 1937—There was a tilting forward of the lower end of the upper fragment which was controlled by placing a pin against its anterior cortex.

Postoperative Notes—December 16, 1937. Thirty-six days after the beginning of lengthening, two inches had been gained. The alignment was satisfactory together with the formation of some callus. The knee was being gradually extended with the lengthening apparatus in position.

September 1, 1938—The gain in length of two inches has been maintained with good alignment. Sufficient callus did not form to insure union. A bone graft was performed at the site of the lengthening operation in order to reinforce the callus. The patient remains in the hospital and an end-result cannot be given at this time.

Appended is a description, in detail, of the anatomic dissections which were employed. In some instances these dissections were carried out completely, and in others, only partially. We have also discussed a method of performing an osteotomy of the tibia in the vertical plane. In our opinion, this type of osteotomy provides for the maximum retention of the origin of muscles to the descending fragments with minimum separation of the periosteum. It also preserves the nutrient vessels of the tibia and fibula.

Description of the Dissections in the Above Operation—First Stage. The incision commences over the tendon of the biceps femoris on the posterolateral aspect of the knee and is carried downward along the course of this tendon to the neck of the fibula. From thence it curves obliquely across the anterolateral aspect of the leg to a point about one inch below the level of the tibial tubercle; there, it follows the crest of the tibia to the junction of the middle and lower thirds of the leg (Fig. 7 a). In general, the incision follows the course of the common peroneal nerve in its upper part and the anterior tibial vessels and nerve in their lower parts. The common peroneal nerve is immediately exposed under cover of the medial border of the biceps tendon. It is then traced to the lateral aspect of the neck of the fibula where it is firmly

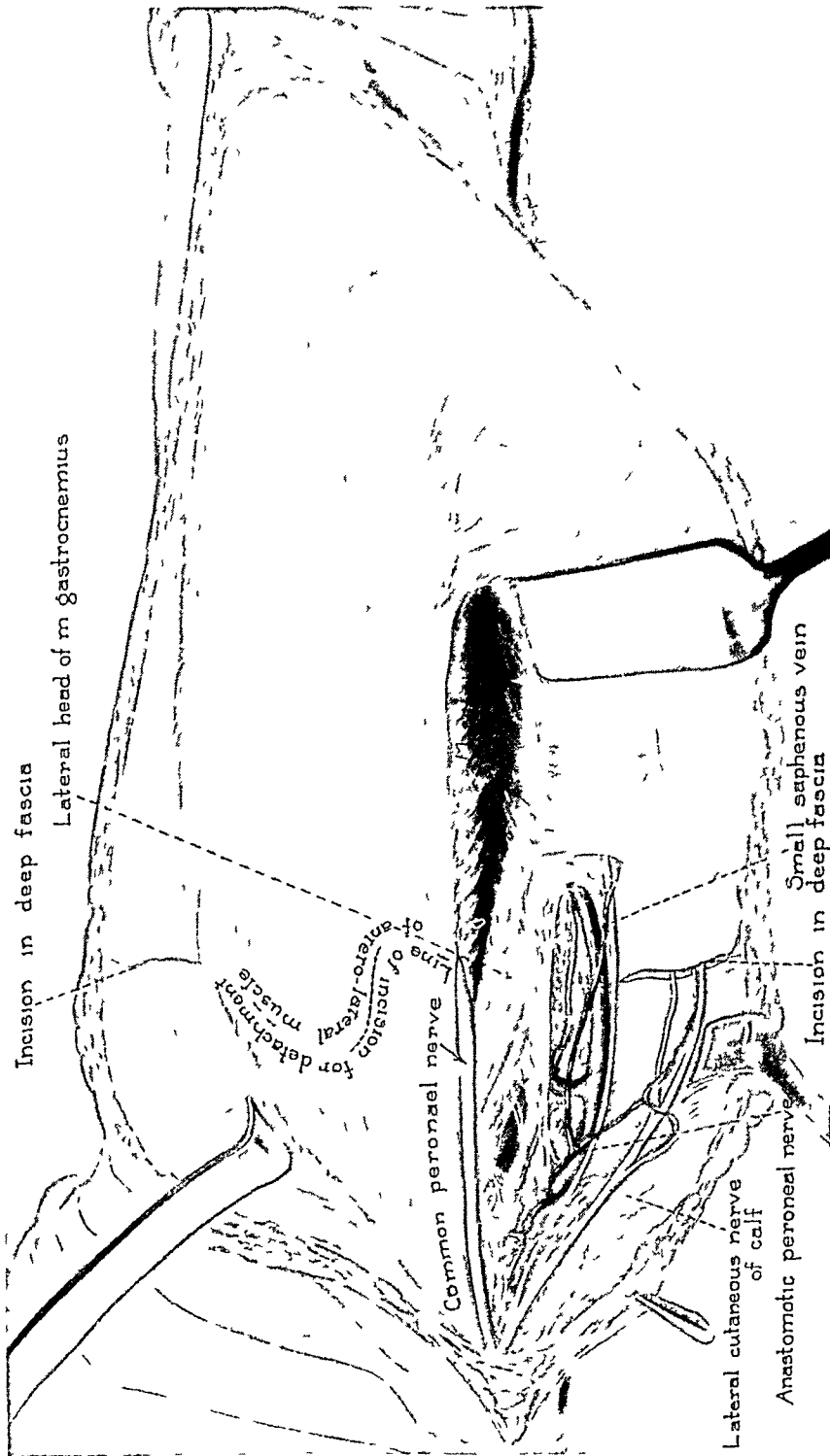


FIG 7(b) —First stage Illustration shows the cutaneous structures. No e method of dividing deep fascia and line of detachment of origin of muscles

LENGTHENING OF TIBIA AND FIBULA

bound down by fascial extensions from the biceps tendon to the deep fascia of the leg. Incision of this fascia constitutes an important step because it frees the nerve from its main point of fixation. Flexion of the knee will now demonstrate a very considerable laxity of the nerve, amounting to as much as one and one-half inches. The nerve can then be readily followed to its division into three chief branches, the upper being the recurrent articular, the intermediate, the deep peroneal and the lower, the superficial peroneal. These branches with their subdivisions are now traced to their entrance into the muscles. In dissecting this nerve, it is well to look for the lateral cutaneous and the anastomotic peroneal branches where they are given off the main trunk

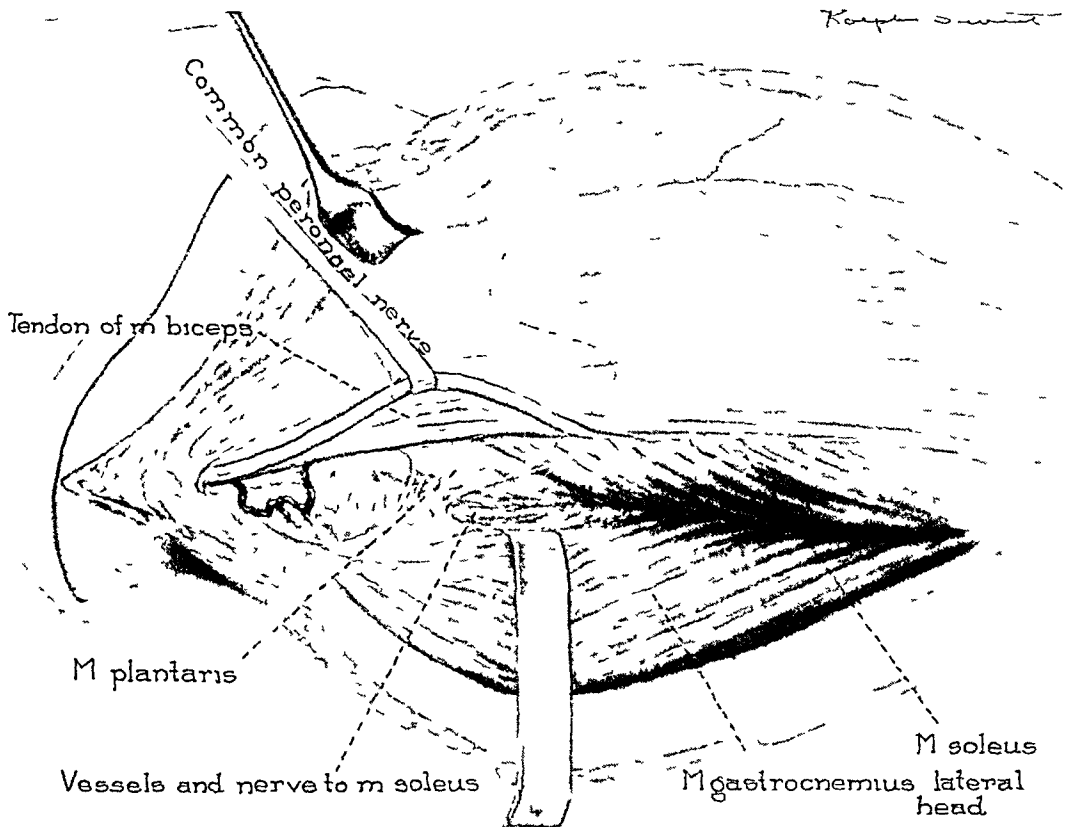


FIG 7(c) —First stage Dissection carried posterior to the fibula with exposure of nerves and vessels to soleus

about two finger breadths above the external condyle, either separately or from a parent trunk. The deep fascia is incised transversely as far laterally as the lesser saphenous vein, taking care to avoid injury to the cutaneous nerves, *i.e.*, the lateral cutaneous nerve of the calf and the anastomotic peroneal nerve (Fig 7 b)

Behind the head and neck of the fibula, the dissection is carried to the lateral head of the gastrocnemius (Fig 7 c). This muscle is retracted posteriorly, exposing the origin of the soleus from the posterior aspect of the head and neck of the fibula. Its nerve and vessel supply may be seen entering its superficial surface near its upper border. The plantaris muscle is identified deep to the medial margin of the lateral head of the gastrocnemius. The plantaris is an important landmark since the junction of its belly and tendon

lies directly over the major vessels and nerves. These structures should be carefully freed from the surrounding tissues. The popliteal artery is found lying upon the popliteal muscle and at its inferior border, and divides into the anterior and posterior tibial arteries. The finger is inserted beneath the fibrous arch of the soleus and this muscle may be lifted backward while its origin is reflected subperiosteally from the fibula. In freeing this muscle great care is exercised to avoid injury to its nerve supply and the anterior tibial vessels. This is the most critical and delicate stage of the dissection, as when the attachment of the soleus is released from the fibula, the anterior tibial vessels are exposed coming forward through the interosseous membrane. At this point the dissection is carried on to the anterior aspect of the upper end of the

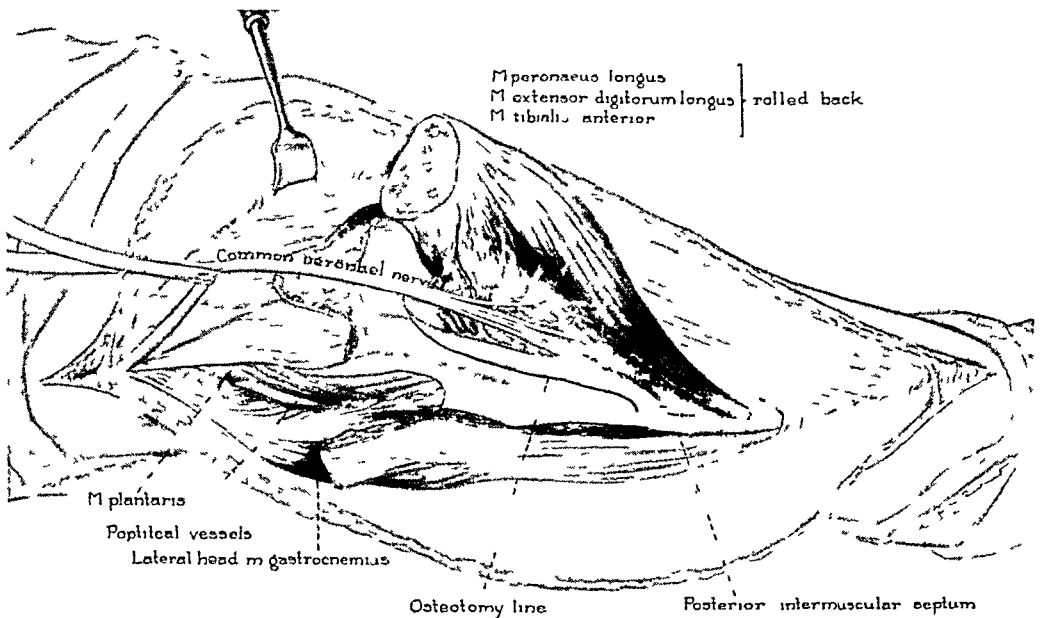


FIG 7(d) —First stage Showing osteotomy of fibula

fibula. The anterior and posterior intermuscular septa are isolated and freely incised. A curved incision is also carried down to the bone across the head of the fibula and along the margin of the attachment of the peroneus longus, extensor digitorum longus and the tibialis anterior muscles to the lateral condyle of the tibia (Fig 7 d). These attachments are deflected with a shaving of bone from the head of the fibula and the lateral condyle of the tibia. As the muscles are turned forward and the common peroneal nerve lifted out of the way, the interosseous membrane is reached from its anterior aspect. The anterior tibial vessels are met with again in the extensor compartment. The interosseous membrane and the tibialis posterior are separated from the upper end of the fibula. The popliteal vessel can now be retracted freely backward because its divisions have been freed at their points of fixation to the interosseous membrane and the fibrous arch of the soleus.

The next step is the division of the bone. A special retractor is passed around the medial surface of the neck of the fibula to protect the blood vessels

LENGTHENING OF TIBIA AND FIBULA

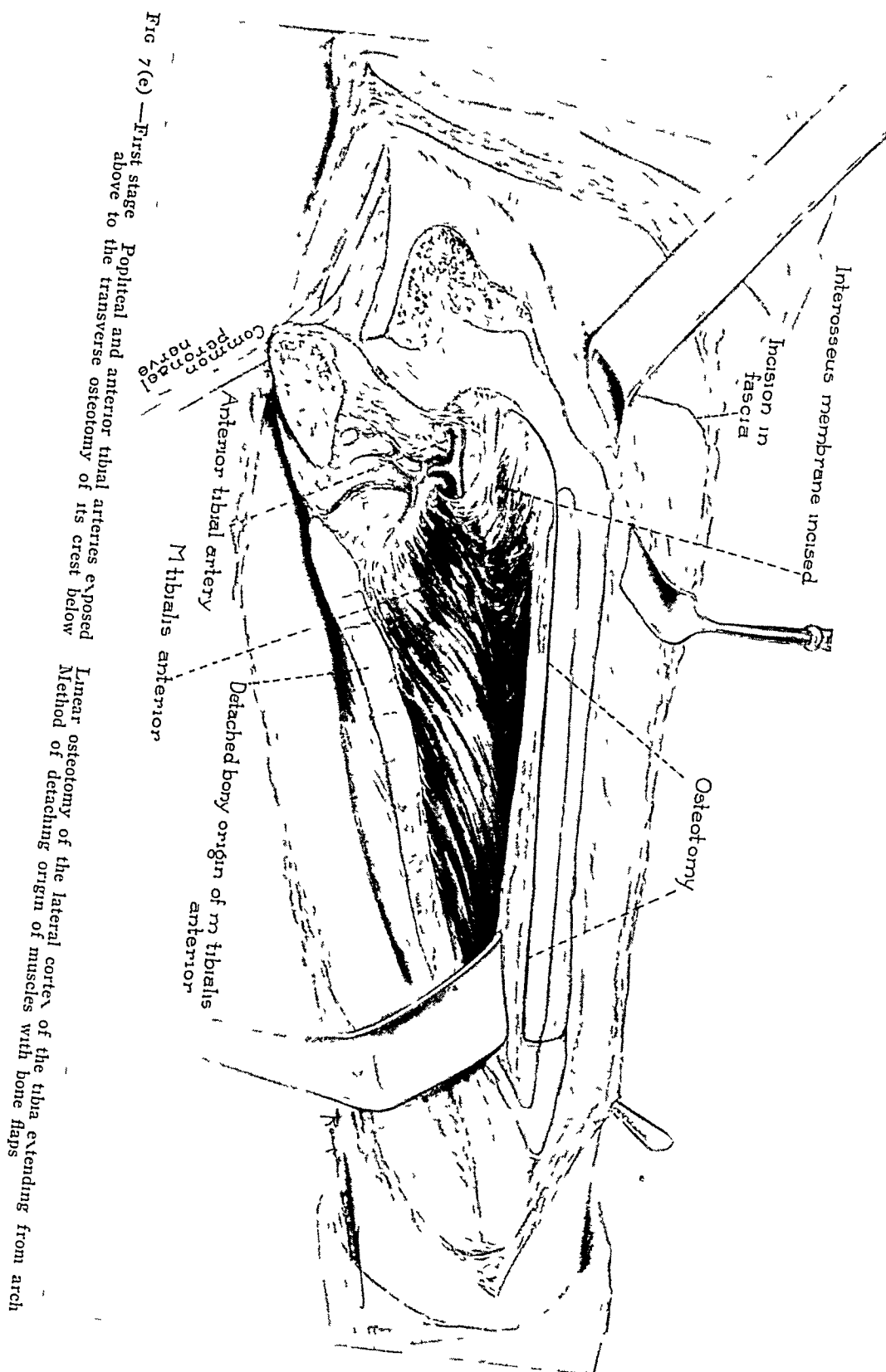


Fig 7(e) —First stage Popliteal and anterior tibial arteries exposed above to the transverse osteotomy of its crest below

Linear osteotomy of the lateral cortex of the tibia extending from arch Method of detaching origin of muscles with bone flaps

and nerves The common peroneal nerve is retracted upward and forward The fibula is sectioned obliquely by a saw cut or by drill and osteotome The osteotomy, about two and one-half inches in length, begins one-half inch below the tibiofibular joint and extends downward and laterally With a saw, or if the operator prefers, a drill, a long oblique section is made through the outer cortex of the tibia This section begins about one-half inch below the apex of the arch and passes downward and gradually forward upon the antero-lateral surface of the tibia until it lies just below the tubercle of the tibia and posterior to the crest At this point, a vertical section of the bone is continued down to the level of the junction of the middle and lower thirds of the bone At the lower end of this section, a transverse osteotomy is made through the crest and cortex of the subcutaneous surface of the tibia (Fig 7 e)

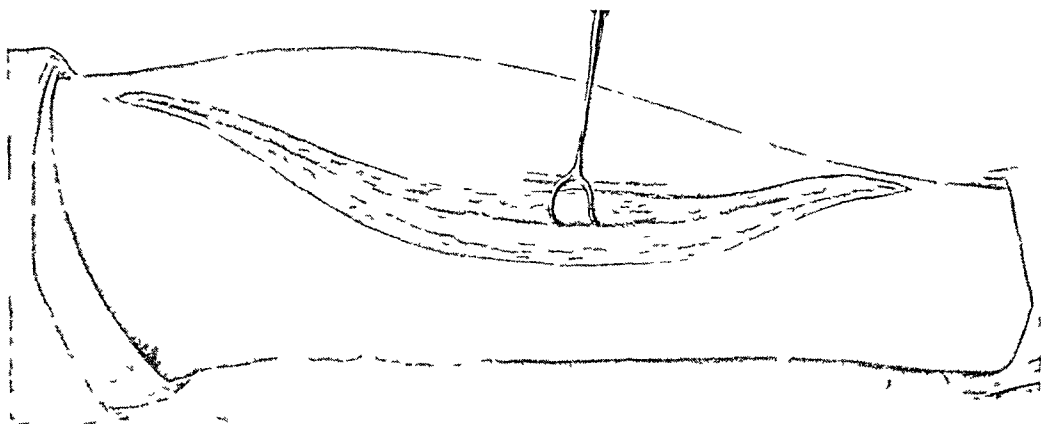


FIG 8(a) —Dissection illustrating anatomic approach through posteromedial incision (second stage)
Curvilinear incision, posteromedial aspect of leg

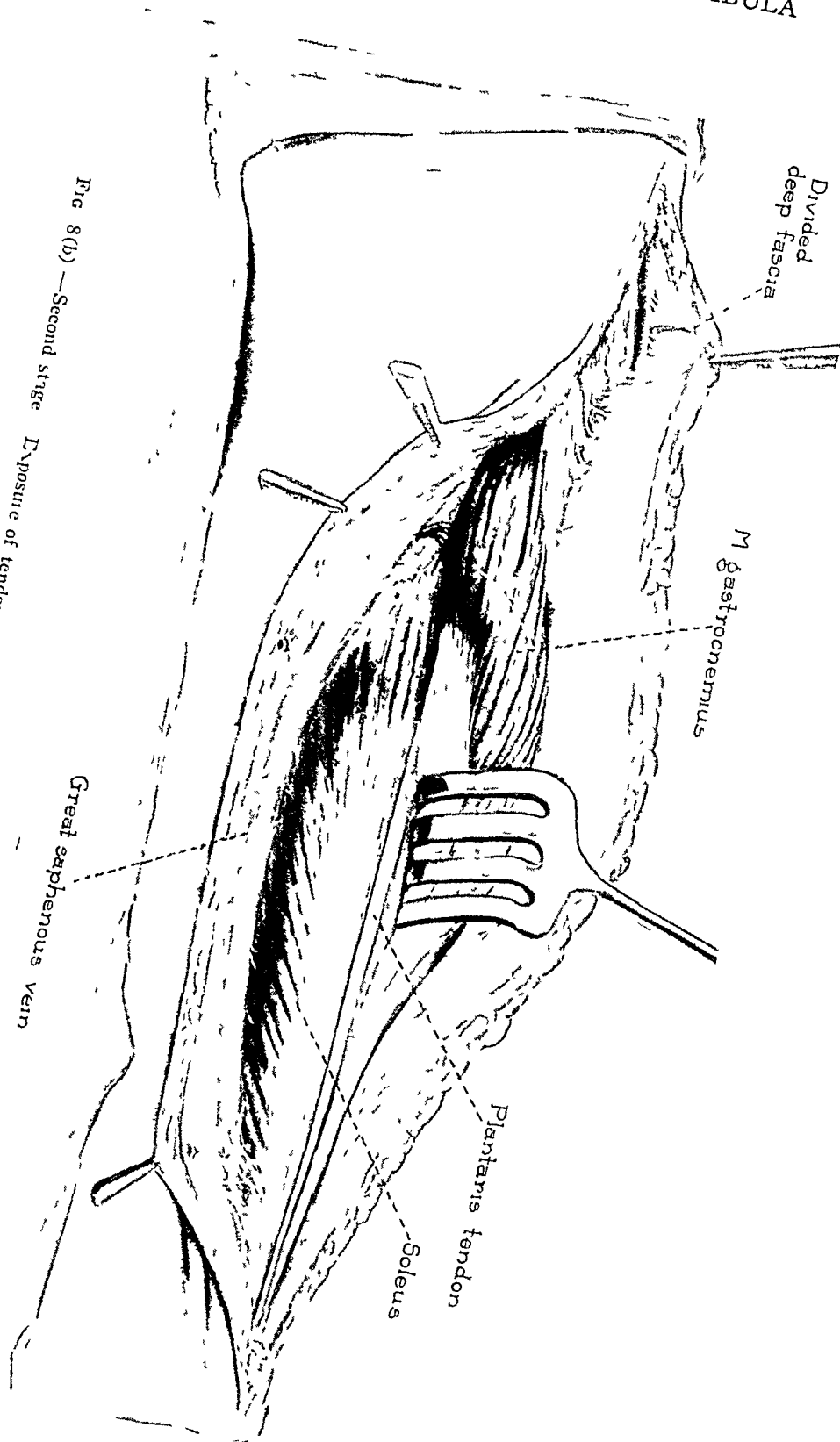
The first stage is completed with suture of the detached origin of the muscles to the surrounding tissues to obliterate the dead space The anterior margin of the peroneus longus and the lateral margin of the soleus are sutured to prevent contact of the common peroneal nerve with the fibula

Second Stage —The lengthening apparatus with the oblique pins is applied With the knee flexed to 30° and externally rotated, a curvilinear incision is made over the posteromedial aspect of the calf It begins over the origin of the inner head of the gastrocnemius and ends at the junction of the middle and lower thirds of the leg where the tendons of the gastrocnemius and soleus merge to form the tendo achillis The summit of the convexity is placed one-half inch behind the medial border of the tibia This avoids injury to the greater saphenous vein and the saphenous nerve (Fig 8 a)

A few veins are ligated as they cross the wound in the subcutaneous tissue The deep fascia is incised along the line of the skin incision At the upper end of this fascial incision, a transverse division is made in the lateral direction through the deep fascia to the margin of the small saphenous vein This transverse division of the fascia meets with the transverse division of the fascia made in the first stage At the lower margin of the wound a similar transverse

LENGTHENING OF TIBIA AND FIBULA

FIG. 8(b) — Second stage Exposure of tendon of gastrocnemius and soleus Note division of deep fascia



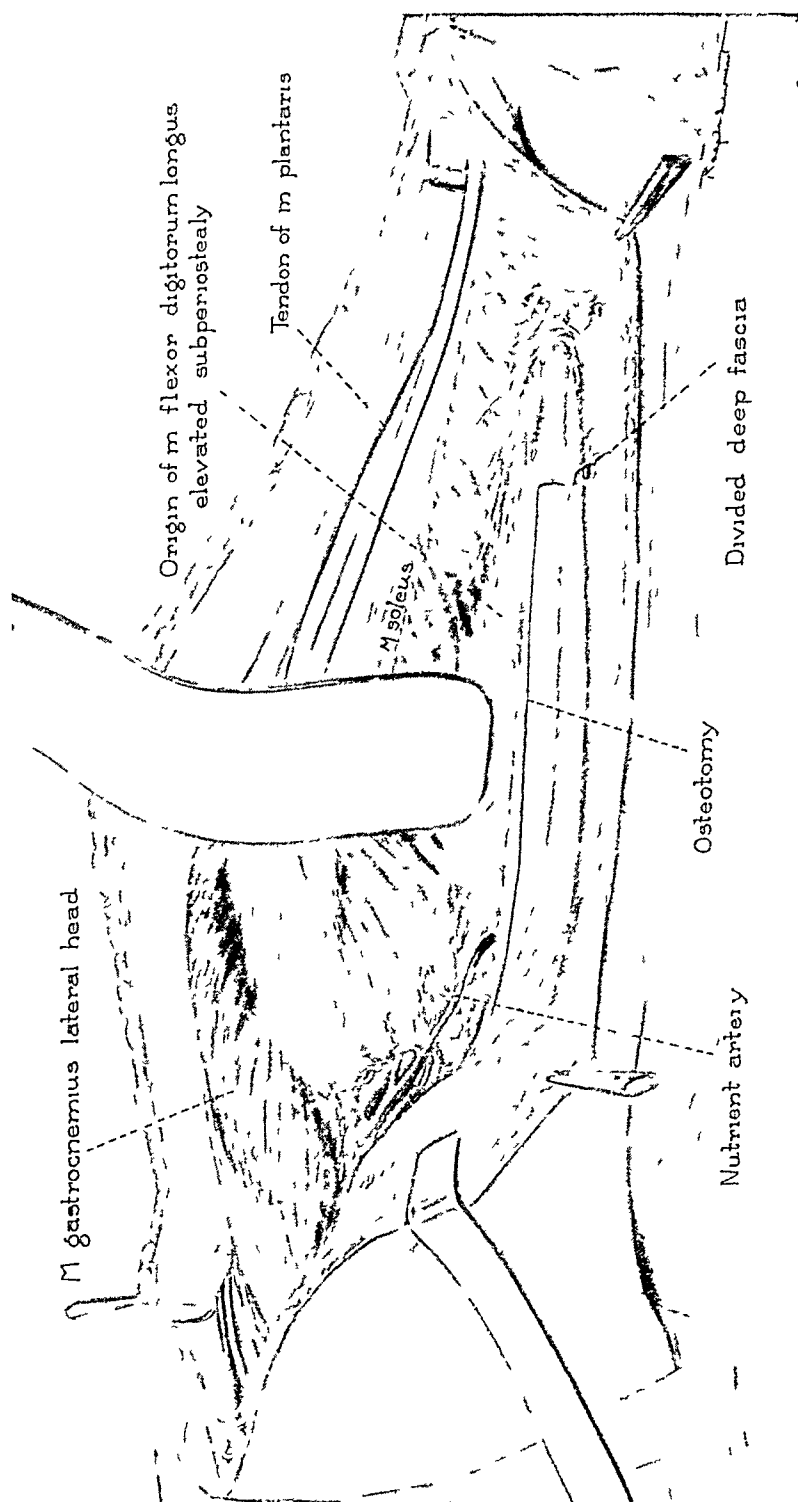


FIG 8(c) —Second stage Osteotomy of tibia showing nutrient vessel

LENGTHENING OF TIBIA AND FIBULA

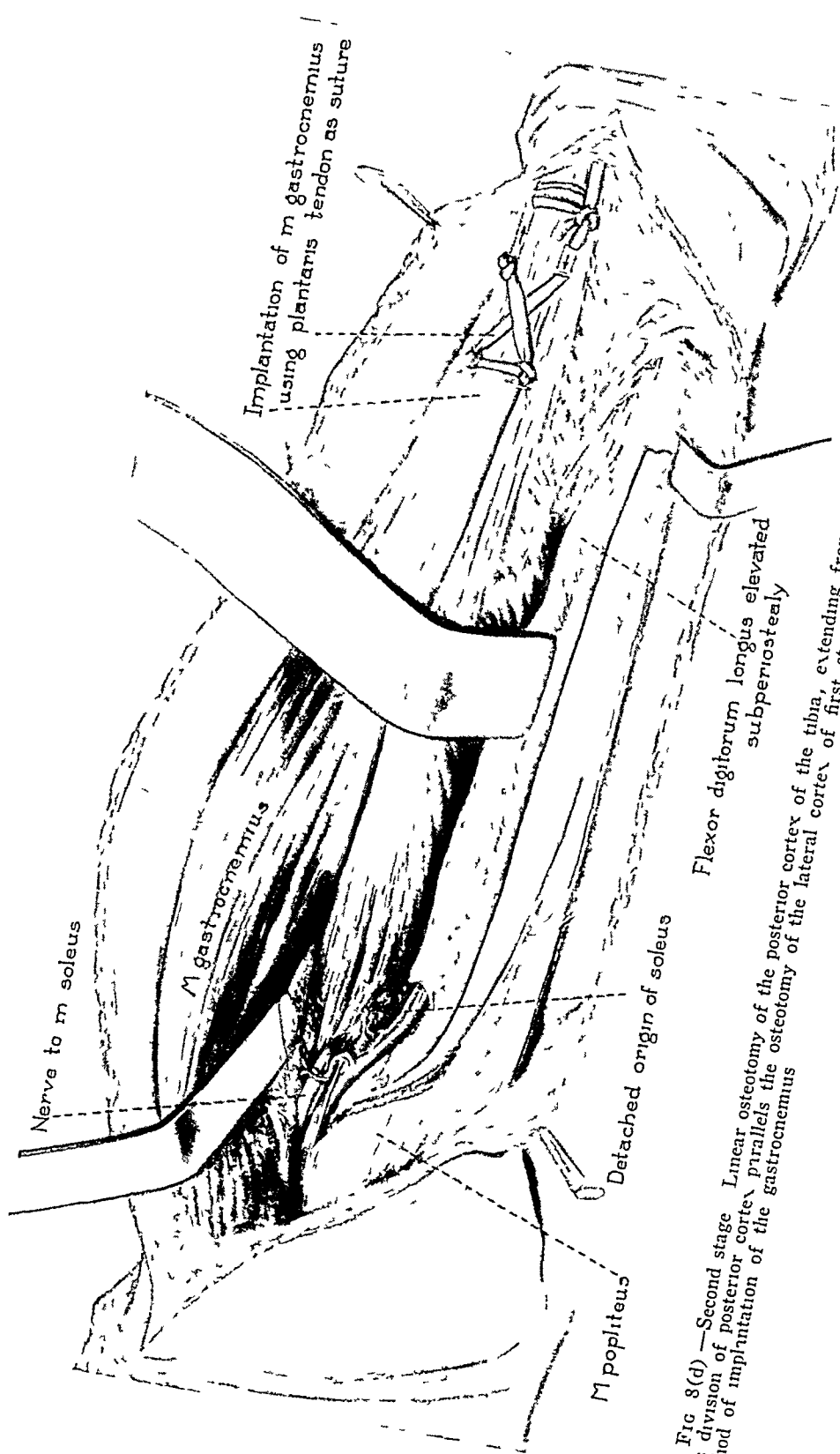


FIG 8(d) —Second stage
This division of posterior cortex parallels the osteotomy of the gastrocnemius
Method of implantation of the gastrocnemius
Extending from arch above to transverse osteotomy below
Completing the separation of the fragments

incision of the fascia is made in an anterior direction until it meets the transverse division of the periosteum on the subcutaneous surface of the tibia at the level of the transverse osteotomy. The fascial incisions of the first and second stages of operation, together with the division of the periosteum, complete an oblique circumferential section of the fascia and periosteum. The tendon of the gastrocnemius is freed from the tendon of the soleus and sectioned obliquely (Fig 8 b). This tendon is then implanted into the soleus at a higher level. The distance upward of this transplantation is equal to the amount of length desired. Here, it is secured by silk sutures which are reinforced by the tendon of the plantaris, this being utilized as a living suture (Fig 8 d). With retraction of the gastrocnemius, the popliteal vessels and the tibial nerves are freed to expose the origin of the muscles in the region of the fibrous bony arch formed by the upper ends of the tibia and fibula.

The soleus muscle is detached at its origin from the posterior aspect and internal border of the tibia, removing with it the superficial layer of the cortex (Fig 8 c and d). As this muscle is turned downward, care should be taken not to injure the popliteal vessels, the tibial nerve and the branches of supply to the soleus and the tibialis posterior. The nutrient vessels of the tibia, associated with the muscular branches of the soleus, are found entering the bone obliquely an inch or two below the oblique popliteal line on the lateral side of the posterior surface of the shaft. The insertion of the popliteus is reflected upward from the oblique line sufficiently to expose the posterior border of the tibia as it ascends to the apex of the arch. At this place, the origin of the tibialis posterior and the attachment of the interosseous membrane are freed for a distance of one and one-half inches. In this denuded area a special retractor is inserted protecting the main vessels and nerves, while the bone is sectioned with a drill or saw, beginning one-half inch below the tibiofibular arch. The osteotomy through the posterior cortex parallels at first the oblique line and then passes down just lateral to the medial border of its shaft to the junction of the middle and lower thirds where it meets the posterior extremity of the transverse osteotomy of the first stage of the operation (Fig 8 d). Care is taken to insure that the fragments are free. The extension apparatus is now tightened until one can see a distinct separation of the fragments. The wounds are closed and the leg is supported in flexion.

Case 7—P. E., male, age 16. Admitted, December 27, 1937.

Chief Complaint—Shortening of the left leg.

History—The patient had tuberculosis of the left hip at the age of two. There were draining sinuses at the site of the infection. He had an arthrodesis of the left hip December 31, 1925. He had a second arthrodesis of the left hip April 13, 1929, and an osteotomy of the left femur November 3, 1932. The sinuses had stopped draining since August, 1932.

Physical Examination—The left hip was arthrodesed in a position of slight abduction. There was about 20° flexion. The knee was markedly unstable. It presented about 10° valgus deformity which could be increased to 30°. Flexion of the knee was possible to 90°. The knee could be completely extended. There were four and one-half inches of shortening in the tibia and fibula and one-half inch of shortening in the femur.

Operations—December 31, 1937, and January 17, 1938. These were performed in two

stages The osteotomy of the tibia and fibula was performed in the anteroposterior plane as described above The oblique pin apparatus was applied

Postoperative Notes—The lengthening process was begun 10 days after the completion of the second stage It was continued until February 21, 1938, when there was a gain of two and one-half inches

March 10, 1938—The apparatus was removed and a Mathews wire was passed through the os calcis The ends of this wire were incorporated in a plaster encasement which extended from the toes to the groin He was discharged April 29, 1938

COMMENT—The patient was examined at intervals, and at the time of his last examination, October 9, 1938, he was bearing weight with the aid of a plaster encasement for protection There was good alignment with bony union and a gain of two and one-half inches in length There was no deformity of the foot or ankle and the tarsal joints had free motion in all directions He had excellent power in the muscles whose origins were freed (Fig 9)

This case demonstrates that the freeing of the origins of the muscles to permit adequate lengthening does not interfere with the retaining of their functions The absence of deformity of the foot, ankle and at the site of osteotomy was a striking feature in this case

Postoperative Lengthening—The lengthening process is carried out in much the same manner as described in earlier publications Our experience has shown that one-sixteenth of an inch of length per day can be gained with little discomfort to the patient In a few instances, we have increased the rate of lengthening to one-eighth of an inch per day and, in one case, gained one and one-half inches in 20

days We do not recommend this manner of rapid lengthening, however, because it generally causes considerable pain Daily measurements are recorded and roentgenograms are taken at intervals to check the position of the fragments and the amount of callus which has formed Usually, sufficient callus has developed in 10 to 12 weeks to permit gradual extension of the knee In some cases we have used a supporting splint which was devised by our instrument and brace-maker, Mr August Keim, which adequately supports and allows minute adjustments during the lengthening and during the gradual extension of the knee When the knee has been completely extended, the apparatus is removed and the leg is immobilized in a plaster encasement which extends from the toes to the groin Weight-bearing with support is generally allowed in four or five months To lessen the chances of fracture, we have insisted on the use of a protective weight-bearing appliance until the callus is



FIG 9—Case 7 showing length secured, with good alignment and formation of callus Note the bridge of new bone forming where the muscles were detached from the arch formed by the upper ends of the tibia and fibula

completely formed with restoration of the medullary canal, a period usually of nine to 12 months

SUMMARY AND CONCLUSIONS

The writers have described a technic of operation for lengthening of the tibia and fibula which is based on new principles

(1) These principles involve complete division of the deep fascia of the leg, the intermuscular septa and the interosseous membrane, as well as the freeing of all of the important blood vessels and nerves at the upper portion of the leg

(2) Special osteotomies have been devised, which provide for retention of the maximum portion of the origin of the muscles which pass from the leg to the foot and permit them to travel downward with the descending fragments

(3) Incisions provide for freeing the blood vessels and nerves from their points of fixation, thus permitting relaxation of these structures during the lengthening. The operation also provides for the preservation of the nutrient vessels of the tibia and fibula, and with the minimum reflection of the periosteum there is but little disturbance of the blood supply to these bones

(4) A new apparatus has been developed which we believe will give better control of the fragments, and offer less chance of infection of the pin wounds

(5) Our recent operations comprise seven cases, all of which have been handled in a somewhat different manner

(6) As a result of our practical experience, we feel that the operation is based on sound principles, all designed to avoid complications which are certain to occur in some instances with the previous methods described

(7) In the seven cases studied with the newer methods which we have devised, the anterior tilting of the upper fragment has been decidedly less marked and we believe it will be entirely controlled by flexion of the knee together with the recent method of transplantation of the gastrocnemius tendon. The internal bowing of the fragments of the tibia and the deformities of the knee and foot have been almost entirely eliminated. No important changes have been noted which could be attributed to injury to the blood vessels or nerves

(8) We emphasize that the operation of leg lengthening is and in all probability always will be, a major undertaking with the possibility of serious complications. The procedure demands an intimate knowledge of anatomy, a careful study of every stage of the operation and postoperative care. We believe that this is not an operation for the uninitiated and should be reserved for those whose experience renders them competent to perform this technically difficult and delicate procedure. In its present stage of development, no final conclusions are offered. We would advise, however, that no one should attempt it without carefully reviewing every detail of our work and then supplementing it with a thorough anatomic study

(9) In the beginning of our work on bone lengthening, we designed procedures which were conservative in character. Recently, we have carried

out more radical operations to avoid complications which arise with these methods. We are convinced that with further study and experience, a middle course will be found which will swing the pendulum again toward conservatism but at the same time will permit the attainment of the objectives desired.

REFERENCES

- ¹ Abbott, L. C. The Operative Lengthening of the Tibia and Fibula. *Jour. Bone and Joint Surg.*, 9, 128, January, 1927.
- ² Abbott, L. C., and Crego, C. H. The Operative Lengthening of the Femur. *Southern Med. Jour.*, 21, 823, 1928.
- ³ Abbott, L. C. Lengthening of the Lower Extremities. *Calif. and West. Med.*, 36, 6, 1932.
- ⁴ Abbott, L. C., Crego, C. H. and Adams, A. C. The Operative Lengthening of the Lower Extremities. *Internat. Jour. Orthodontia*, 15, 110, 1929.
- ⁵ Brockway, A. Clinical Resume of 46 Leg Lengthening Operations. *Jour. Bone and Joint Surg.*, 17 (No. 4), 969, October, 1935.
- ⁶ Phemister, D. B. Operative Arrestment of Longitudinal Growth of Bones in the Treatment of Deformities. *Jour. Bone and Joint Surg.*, 15 (No. 1), 1, January, 1933.
- ⁷ White, J. W. Femoral Shortening for Equalization of Leg Length. *Jour. Bone and Joint Surg.*, 17 (No. 3), 597, July, 1935.
- ⁸ Compere, E. L. Indications for and against the Leg Lengthening Operation. *Jour. Bone and Joint Surg.*, 18 (No. 3), 692, July, 1936.
- ⁹ Haboush, E. J., and Finkelstein, E. Leg Lengthening with New Stabilizing Apparatus. *New York Jour. Bone and Joint Surg.*, 14 (No. 4), 807, October, 1932.

TABLE II

PATHOLOGIC CONDITIONS ASSOCIATED WITH LENGTHENING OF AN EXTREMITY

- (A) Congenital Conditions
 - (1) Hemihypertrophy
 - (2) Arteriovenous aneurysm
 - (3) Recurring hemarthrosis in hemophilia
- (B) Infections
 - (1) Tuberculosis of knee (low grade)
 - (2) Chronic osteomyelitis of femur or tibia
 - (3) Chronic soft tissue infection
 - (4) Syphilis
 - (5) Femoral or iliac thrombosis
 - (6) Elephantiasis
- (C) Tumors
 - (1) Giant cell tumor
 - (2) Osteitis fibrosa cystica (diffuse unilateral type)
 - (3) Neurofibromatosis (von Recklinghausen)
 - (4) Hemangioma or lymphangioma
 - (5) Large nevi
- (D) Trauma
 - (1) Fracture of femur
 - (2) Removal of bone graft from tibia
 - (3) Extensive periosteal stripping

Ollier,⁴⁶ in 1867, noted that irritation of the shaft of a bone produced acceleration in the rate of growth, and Kishikawa⁴⁰ found that ligation of the femoral vein, or injection of oil of turpentine into the marrow cavity, caused slight but definite increase in the growth rate. Meisenbach,⁴³ Bohlman¹⁵ and others inserted numerous foreign materials into the region of the epiphyseal cartilage with the object of producing more rapid bone growth through local irritation. However, most of these substances caused retardation, and none of them accomplished the desired result. When the material inserted was definitely irritating or caustic there was often complete disappearance of the epiphyseal line. Brooks¹⁸ found that small doses of roentgen ray (2 to 5 per cent S E D) caused no stimulation. The most successful experiments were those of Wu and Miltner,⁶² who produced an increase of 5 to 15 per cent in the growth rate of the extremities of young animals by extensive periosteal stripping.

Increased longitudinal growth following fracture of a growing bone has been noted clinically and experimentally. It cannot be considered compensatory as it commonly occurs even though there is no shortening due to the fracture. Ferguson³¹ believed that the interruption of the metaphyseal blood supply with resulting hyperemia in the epiphyseal region was the cause of this increased growth rate. Based upon this assumption, stimulation of growth was attempted in a number of patients by drilling the cortex near the epiphysis and curetting across the marrow cavity. A gain of one-twelfth to one-eighth of an inch was reported three to five months after operation.

Wu and Miltner,⁶² and Compere and Adams²⁷ were unable to produce, experimentally, any stimulation of bone growth by the method advocated by

Ferguson Brockway,¹⁹ Chandler,²³ and Compere and Adams observed definitely increased growth in normal tibiae from which a graft had been removed. The latter two, after an extensive experimental and clinical study, concluded that gross trauma involving a considerable portion of a long bone and requiring a lengthy period of repair was the inciting factor. In their opinion the increased growth rate was directly associated with the local hyperemia and continued only during the period of increased vascularity.

The problem of producing an increased blood supply over a prolonged period presents great difficulties. Lumbar sympathectomy apparently accomplishes this better than any local procedure yet devised. Although the experimental attempts to stimulate growth by lumbar sympathectomy in animals have been uniformly unsuccessful, in children it is known to produce a lasting hyperemia, and many of these patients show definite gain in the rate of growth on the operated side. Stewart⁵⁵ noted one-half of an inch lengthening in two out of six patients who had had unilateral sympathectomy for spastic hemiplegia. Harris and McDonald³⁶ reported increased growth of one-half to one inch in three patients upon whom unilateral sympathectomy had been performed for Hirschsprung's disease.

These authors examined 46 out of 100 patients with poliomyelitis, who had had unilateral lumbar sympathectomy to improve circulation and stimulate growth. They stated that there was always some increase in the growth rate. In 21 of these, the improved vascularity resulted in a decrease in the discrepancy between the two extremities. This decrease amounted to one inch in two instances, three-quarters of an inch in four, and in the other 15 it was one-half of an inch or less. In eight, the hyperemia was sufficient to prevent any further increase in discrepancy. In 17, the discrepancy between the two extremities increased, but less rapidly than before the operation. According to these authors there is a basic rate of growth which in normal legs is stimulated by normal muscle activity and a normal blood supply. Sympathectomy improves only the latter and is not very effective in a severely paralyzed extremity. There are probably other factors such as diminished weight bearing which influence the leg growth after paralysis. It is even possible that there is a direct control of growth by special cells in the central nervous system, and that these, as well as the anterior horn cells, are affected by the virus of poliomyelitis.

Although lumbar sympathectomy may produce a prolonged hyperemia and is well worth while for the relief of chilblain and pain associated with poor circulation, the increase in growth is too little and too inconstant to recommend it as a method of equalizing leg lengths.

At the Hospital for Ruptured and Crippled, a small number of paralytic cases have been treated with diathermy to the epiphyses about the knee of the shorter extremity. In several instances there has been no further increase in the discrepancy between the two legs. Even if these treatments could be given daily or twice daily for a period of years, one would hardly expect as much improvement as from lumbar sympathectomy. We must, therefore, conclude that attempts to stimulate epiphyseal growth have not

been successful enough up to this time to warrant their clinical application

(2) *Retardation of Growth in the Longer Extremity*—Diminution or complete cessation of longitudinal growth occurs even more commonly than increased growth. The same abnormal conditions which cause stimulation frequently cause retardation, especially if the pathologic process actually involves the epiphyseal line. Any lesion associated with diminished circulation or gross trauma to the region of the growing cartilage disk is apt to produce partial or complete arrest of growth (Table III). Uneven growth with angular deformity is even more serious than uniform shortening.

TABLE III

PATHOLOGIC CONDITIONS ASSOCIATED WITH SHORTENING OF AN EXTREMITY

- (A) Congenital Conditions
 - (1) Unreduced congenital dislocation of hip
 - (2) Congenital absence or partial absence of a long bone
 - (3) Congenital hemiatrophy
 - (4) Chondrodysplasia
 - (5) Other congenital anomalies
- (B) Infections
 - (1) Poliomyelitis
 - (2) Tuberculosis of hip or knee
 - (3) Suppurative arthritis of hip, knee, or ankle
 - (4) Osteomyelitis of femur or tibia
- (C) Tumors
 - (1) Osteitis fibrosa cystica (diffuse type)
 - (2) Osteochondroma
 - (3) Giant cell tumors
 - (4) Other tumors
- (D) Trauma
 - (1) Slipping of upper femoral epiphysis
 - (2) Other epiphyseal separations
 - (3) Fractures involving epiphyseal cartilage disks
 - (4) Operative trauma to epiphysis
 - (5) Roentgenotherapy for conditions near the epiphyseal line
 - (6) Malunited fractures

Although short extremities and growth deformities of the bones have been observed for years, Phemister⁴⁹ was the first intentionally to limit longitudinal bone growth by surgical means. He described a simple procedure which consisted of removing small bone grafts from each side of the lower end of the femur or the upper end of the tibia. These were taken largely from the diaphysis but extended just across the epiphyseal line. The epiphyseal cartilage plate was exposed by this removal and a large area of it curetted. The grafts were turned end-for-end and reinserted across the epiphyseal line. No postoperative support was required. Compere²⁵ stated that this operation had been performed in more than 100 cases at the University of Chicago Clinics, without complications.

Brooks¹⁸ and others have shown that proliferation of the cartilage cells of the epiphyseal line can be delayed or even completely inhibited by exposure to roentgen rays. No attempt has been made to apply this method clinically, as serious damage to the adjacent articular structures is almost inevitable.

Many of the attempts to stimulate bone growth, contrary to expectations, produced retardation or even complete cessation, and it is possible that some method of epiphyseal arrest, even simpler than that of Phemister, may yet be evolved.

Although late deformities have not been reported, we have encountered three patients operated upon according to Phemister's technic who developed disalignment at the knee sufficient to require operative correction. In experimental animals, attempts to arrest growth by his and other methods frequently resulted in severe lateral deformity. In a series of 25 rabbits, we were able to produce uniform and complete arrest of growth only when a considerable part of each side of the cartilage disk was removed and the remaining cells in this area destroyed by electrical cauterization (Fig 1). With this combined procedure complete cessation of growth occurred either with or without the cortical graft across the epiphyseal line.

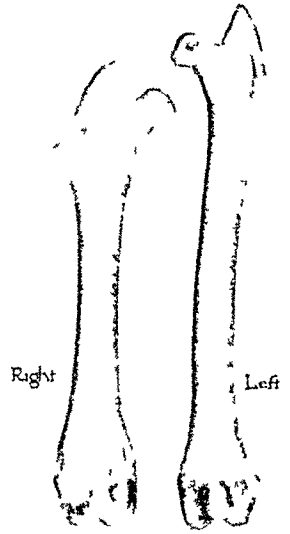


FIG 1—Rabbit bones after epiphyseal fusion on right, showing amount of shortening obtained

At the Hospital for the Ruptured and Crippled, during the past four years, 34 operations for the retardation of growth have been performed upon 30 patients, with no infections and no postoperative deformities or other complications. The essential points of the technic are (Fig 2)

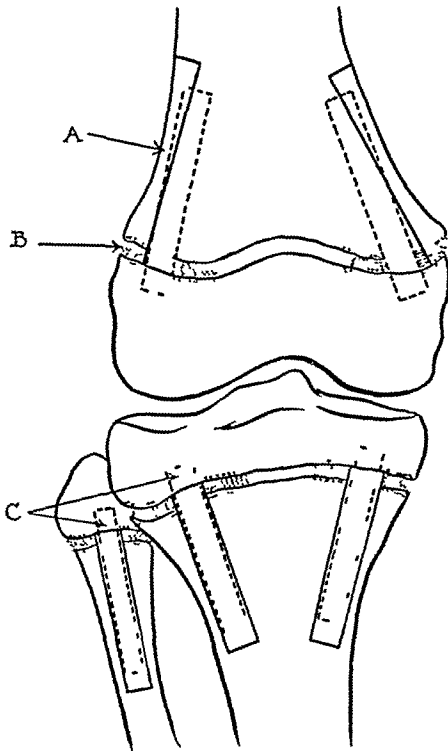


FIG 2—Diagram of operative technic for epiphyseodesis. (A) Bone removed for graft. (B) Area of epiphyseal cartilage curetted and cauterized. (C) Replacement of graft with cartilage removed, across epiphyseal line.

(1) The medial and lateral sides of the lower end of the femur or upper end of the tibia and fibula are exposed through separate incisions.

(2) Bone grafts, about 1x4 cm in size, are removed from the diaphysis. These extend as far as, but not across, the epiphyseal cartilage plate.

(3) A large area from both the medial and lateral aspects of the cartilage disk is removed with a chisel or curet.

(4) The curetted area is cauterized with the diathermy cautery.

(5) The grafts are replaced, countersunk beneath the cortex of the diaphysis, and driven across the epiphyseal line into the cancellous bone of the epiphysis.

More difficult than the actual technical procedure is the decision as to when the operation should be performed and which epiphyses should be fused. Digby,³⁰ in 1916, determined the proportional

growth at the various epiphyseal lines and his estimations have been confirmed by subsequent clinical observations. Complicated methods for determining the optimum age for operation have been propounded, based upon the average height, leg length, and growth rate at various ages. The authors feel that each patient must be considered individually and decision made upon the basis of previous rate of growth and expected growth in the extremities as well as age, height and leg lengths. Measurements of the patient's family are also of definite assistance. With these considerations in view, and the fact that practically all adults are between five and six feet in height, with a leg length of 30 to 38 inches, it is possible to arrive, with a fair degree of accuracy, at a figure which will represent the expected length of the longer extremity at maturity. Subtracting the present leg length from this figure gives the expected amount of growth in this leg if no treatment is undertaken. As attempts to estimate the growth in the femur and tibia separately only make the problem more complicated, the figures of Digby have been adjusted to apply to total leg length. For all practical purposes the figures shown in Table IV are sufficiently accurate.

TABLE IV
APPROXIMATE PROPORTIONAL GROWTH AT THE
EPIPHYSES OF THE LOWER EXTREMITY

Upper femoral epiphysis	15%
Lower femoral epiphysis	35%
Upper tibial epiphysis	30%
Lower tibial epiphysis	20%

The expected discrepancy can be estimated if records of the leg lengths over a period of years are available. If the discrepancy has not been increasing with growth, the present discrepancy equals the expected discrepancy. If the rate of growth in the longer leg has been greater than in the shorter extremity, the discrepancy will continue to increase proportionately.

If the expected discrepancy is divided by the expected growth in the longer extremity, the proportion of growth which should be eliminated is obtained, thus $\frac{\text{expected discrepancy}}{\text{expected growth}} = \text{per cent of growth to be eliminated}$, for example—(1) If this proportion is less than 25 per cent, operative treatment should be delayed, (2) if it is between 25 and 60 per cent, growth should be arrested at the upper femoral or upper tibial and fibular epiphyses, (3) if it is more than 60 per cent, all the epiphyses at the knee should be fused, (4) if it is more than 70 per cent, complete equalization of leg length by this means cannot be obtained.

If the patient is under ten years of age the arrest of growth at a single epiphysis is preferred and is often sufficient. If the patient grows less than was anticipated and some discrepancy persists, another epiphysis can be fused a year or two later. If only a moderate retardation of growth seems indicated the decision as to whether the operation should be performed above or below the knee depends upon whether the shortening in the opposite extremity is greater in the thigh or lower leg.

It is impossible to report end-results in these cases until growth is complete, 14 patients, however, averaging $12\frac{1}{2}$ years at the time of operation, have been observed from one to four years later. Seven of these showed a lessening in discrepancy of one to one and three-quarters inches. In three, the decrease was one-half to one inch. In two, the difference between the two legs remained the same, while in two, the discrepancy increased slightly despite the operation. Epiphyseal-diaphyseal fusion was accomplished in all cases, and even in those where no equalization of leg length was obtained a rapidly progressive discrepancy was arrested.

ILLUSTRATIVE CASE REPORTS

Case 1—F. B., male, age 14. *Diagnosis* Poliomyelitis in 1924, at the age of one year, resulting in a severe paralysis and marked shortening of the left leg.

Preoperative Measurements

Date	Age	R Leg	L Leg	Difference
3-6-29	5 yrs	22 ins	$20\frac{3}{4}$ ins	$-1\frac{1}{4}$ ins
12-5-34	10 yrs	$29\frac{1}{4}$ ins	$26\frac{1}{4}$ ins	-3 ins
2-5-35	11 yrs	30 ins	27 ins	-3 ins
3-8-37	13 yrs	$34\frac{1}{4}$ ins	$31\frac{1}{4}$ ins	-3 ins

Although the patient had already reached the age of 13, he was still growing rapidly, and as his family were also tall, the normal leg without treatment would probably grow three inches or even four inches more. If the present discrepancy of three inches is divided by the expected growth it is found that 75 to 100 per cent of this growth should be eliminated. On March 10, 1937, growth was arrested at the epiphyses of the lower end of the right femur and the upper end of the right tibia and fibula.



FIG 3—Case F. B. Views of knee 19 months after operative arrest of growth at the lower end of femur and upper end of tibia and fibula. During this period, the discrepancy in length decreased two and one half inches.

Postoperative Measurements

Date	Age	R Leg	L Leg	Difference
9-15-37	13 yrs	34 $\frac{3}{4}$ ins	31 $\frac{1}{2}$ ins	-3 $\frac{1}{4}$ ins
3-15-38	14 yrs	34 $\frac{1}{2}$ ins	32 $\frac{1}{2}$ ins	-2 ins
10-18-38	14 yrs	35 $\frac{1}{2}$ ins	34 $\frac{1}{2}$ ins	-1 in

After operation, the shorter leg grew three and one-quarter inches, while the longer one grew only one and one-quarter inches, showing that growth in the normal leg had been reduced at least 60 per cent

Case 2—J M, female, age 12 *Diagnosis* Poliomyelitis in 1927, at the age of one year, resulting in an extensive paralysis of the left leg

Preoperative Measurements

Date	Age	R Leg	L Leg	Difference
9-1-27	1 yr	13 $\frac{3}{8}$ ins	13 $\frac{3}{8}$ ins	None
9-25-31	5 yrs	20 $\frac{1}{2}$ ins	19 ins	-1 $\frac{1}{2}$ ins
10-25-34	8 yrs	27 $\frac{1}{4}$ ins	25 $\frac{1}{4}$ ins	-2 ins
5-19-36	10 yrs	28 $\frac{1}{2}$ ins	26 $\frac{1}{2}$ ins	-2 ins

The patient's family were all rather short and although the patient was only age 10, she was well developed. It was evident that the normal leg without treatment would not grow more than six inches more. Dividing the discrepancy of two inches by the expected growth showed that at least 33 per cent of this should be eliminated. On May 20, 1936, an operation for arrest of growth was performed at the lower end of the right femur.

Postoperative Measurements

Date	Age	R Leg	L Leg	Difference
10-2-36	10 yrs	28 $\frac{3}{4}$ ins	26 $\frac{3}{4}$ ins	-2 ins
2-26-37	11 yrs	28 $\frac{3}{4}$ ins	27 $\frac{1}{4}$ ins	-1 $\frac{1}{2}$ ins
1-29-38	12 yrs	30 $\frac{1}{4}$ ins	29 ins	-1 $\frac{1}{4}$ ins

Although growth in the right leg had been retarded, there was still a discrepancy of one and one-quarter inches to be overcome. Operative fusion of the epiphyses of the upper end of the tibia and fibula was performed on February 16, 1938.

Postoperative Measurements

Date	Age	R Leg	L Leg	Difference
5-1-38	12 yrs	30 $\frac{3}{4}$ ins	29 $\frac{1}{2}$ ins	-1 $\frac{1}{4}$ ins
9-23-38	12 yrs	31 $\frac{1}{4}$ ins	30 $\frac{1}{4}$ ins	-1 in
12-30-38	13 yrs	32 ins	31 $\frac{1}{2}$ ins	- $\frac{1}{2}$ in

As a result of operations, the growth in the normal extremity has been reduced to three and one-half inches while the short, paralyzed leg was increasing five inches in length.

Review of the published reports and of our own cases leads us to conclude that destruction of the epiphyseal cartilage by operation at the lower end of the femur and/or the upper ends of the tibia and fibula is a simple and safe method of retarding growth. It is to be recommended as an effective means of equalizing leg length during the growing period.

II SURGICAL RECONSTRUCTION—(1) *Bone Lengthening Operations*
Codivilla was the first to devise a method for lengthening a long bone, as well as the first to employ the principle of direct skeletal traction. In 1905, he reported 22 cases, chiefly malunited fractures, in which he had performed an oblique osteotomy and applied traction by means of a pin inserted into the os

calcis He had increased the length by from 3 to 8 cm A firm anatomic foundation for bone lengthening was laid by Magnuson,⁴² in 1908, when he reported the results of experiments in animals which demonstrated that operative lengthening of a normal extremity could be performed without interfering with the blood supply or nerve function

Putti, in 1921,³¹ reported a method for the operative lengthening of the femur, and was the first to make use of the principle of skeletal distraction He first performed a long oblique osteotomy of the femoral shaft and then applied an apparatus consisting of two pins which were inserted from the lateral surface, one into the femoral condyles and the other into the greater

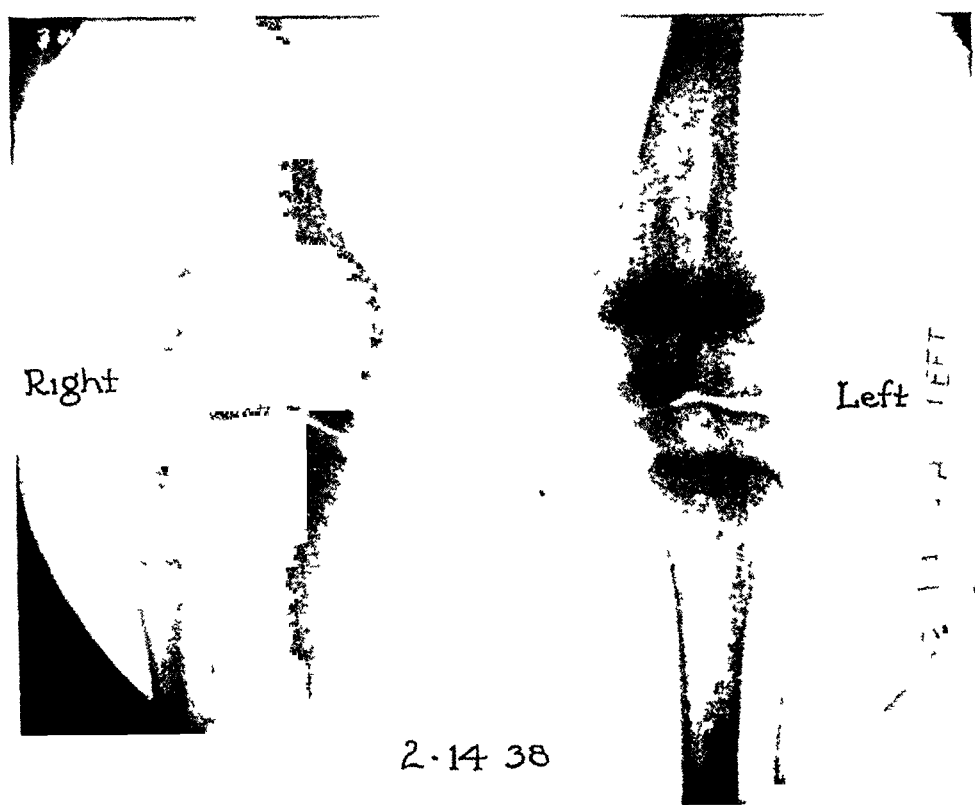


FIG 4—Case J M Roentgenogram taken 21 months after epiphysiodesis at right distal femoral epiphysis Complete fusion has been obtained with three fourths inch correction of discrepancy of length

trochanter, and of a telescoping side-bar which was securely fastened to the protruding ends of the pins and could be gradually lengthened by turning up a screw-thread Putti's method was tried by other surgeons but never became popular because of difficulty in controlling the alignment of the fragments

It remained for L C Abbott¹ to devise a method which put leg lengthening on a practical basis He selected the tibia and fibula as the ideal site for lengthening and after preliminary lengthening of the tendo achillis and oblique division of the shaft of the fibula, he performed a tongue and groove osteotomy of the shaft of the tibia, the tongue being long enough to overlap the other fragment after the desired lengthening had been obtained Pins were passed through the upper and lower ends of the tibia and their projecting ends fixed to rigid, telescoping side-bars on both sides of the leg, the

apparatus when assembled forming a rigid unit and serving as a support for the extremity. Lengthening of approximately one-eighth of an inch a day was obtained by turning up screws until the desired amount was gained. Abbott published the first report of his method in 1927, and it was immediately adopted by other surgeons. He later modified it by employing four pins, two in each fragment to obtain better control of alignment. Other surgeons have devised ingenious modifications of his apparatus, but one and all have employed the same basic principles.

Lengthening of the femur presents more of a problem than that of the bones of the leg, owing chiefly to its deeper situation and stronger muscle attachments which make the control of alignment of the fragments after osteotomy more difficult. Abbott and Crego,² in 1928, described a method with one pin inserted through the condylar region and a second pin passed obliquely downward from the anteromesial aspect of the thigh through the upper third of the shaft and emerging at the posterolateral surface. By means of appropriate apparatus attached to the ends of the pins and also supporting the leg, lengthening was obtained gradually. This method proved too difficult, however, and never became popular. Modifications have been tried and femoral lengthenings are still undertaken, but their number in proportion to lengthenings of the lower leg is relatively small.

From this brief review it will be seen that more than ten years' experience with leg lengthening operations has accumulated, and a fairly accurate evaluation of the procedures can now be made.

A survey of the literature revealed reports by 11 different authors of their experience with leg lengthening operations. Of these, 224 were of the tibia and fibula and 46 of the femur. Lengthening was obtained in all but seven cases, regardless of complications. Average reported gains varied from 1.9 to 2.25 inches. The maximum amount gained from lengthening of one bone was 3.5 inches, but by combined lengthening of the femur and tibia in different stages, as much as 4.5 inches was obtained.

Numerous complications were reported and appeared to be of sufficient frequency and gravity to warrant careful consideration (Table V). Of these, the most disturbing was postoperative infection, which occurred in 22 out of 270 cases, an incidence of 8 per cent. Since several of the authors did not report their complications in detail, it is probable that this figure should be even higher. While it is impossible in this group of cases to separate the infections involving the site of osteotomy, and which were of major significance, from those that were confined to the pin wounds, of only local importance, it is evident that the former occurred entirely too frequently for comfort and are the natural consequences of a procedure that necessitates extensive exposure and traumatization of bone. It is important to point out, however, that only one death was reported in the entire series and aside from this case there were no amputations.

Without doubt, the tendency after tibial lengthening for the fragments to angulate anteriorly, and either protrude directly through the wound or cause necrosis of overlying skin with exposure of the bone, contributed to the high

EQUALIZATION OF LEG LENGTH

Number of
Lengthening
Operations

Tibia
and
Fibula

Remur

Average
Length
Gained
(inches)

Protru-
sion of
Fragments
or Skin
Necrosis

Infection
and
Osteo-
myelitis

De-
layed
Union

Non-
union

Frac-
ture

Nerve
In-
jury

Root
De-
formity

Death

Failure
to
Gain
Length

TABLE V
REPORTED RESULTS OF LEG LENGTHENING OPERATIONS

Complications Reported

Author
Abbott
Stephenson and
Durham
Carrell
Brockway
Janes
Moore, J R
Compere
Besworth
Alcorn
Haboush and
Pinkelstein
Present report

Totals

224

46

2 ins

18

22

5

12

10

5

14+

1

7

2

19 ins

4

5

6

2

3

1

2

4

0

0

19 ins
15 to 2 ins

2

4

6

1

2

3

4

0

1

2

0

1

2

0

0

1003

incidence of infection This difficulty was encountered more frequently in the early experience and was largely overcome by the introduction of the four pin method

Among the other complications reported were fracture of the osteotomy tongue in some instances of tibial lengthening, and separation of the fragments after femoral lengthening These conditions resulted in delayed union when allowed to persist but were generally corrected by secondary operation with insertion of bone grafts to bridge gaps between the fragments and secure union Callus formation and bone healing were delayed in some cases even when there was good approximation of fragments, and several instances of nonunion were reported for which bone grafting operations were necessary Late fractures through the site of the healed osteotomy were not uncommon, as shown by Abbott's report of seven such complications out of 25 femoral lengthenings and occasional mention of similar experiences by other authors after tibial lengthening Nonunion followed some of these fractures

TABLE VI

LEG LENGTHENING OPERATIONS AT THE HOSPITAL FOR RUPTURED AND CRIPPLED

Case	Diagnosis	Short- ening	Length- ening Obtained	Complications	Result at Last Visit
L S	Polio	4 ins	2 $\frac{1}{4}$ ins	Tilting, projection of fragments, osteomyelitis, compound fracture, bone graft, refracture, amputation of leg	4 years later Poor
E W	Old epi- physitis	1 $\frac{1}{2}$ ins Femur	1 in	Tilting of fragments	Not known
P M	Polio	1 $\frac{5}{8}$ ins	2 $\frac{1}{4}$ ins	Slough, projection of fragments, osteomyelitis	3 years later Poor
M H	Polio	1 $\frac{1}{2}$ ins	Lengths equal	None	5 years later Good
H N	Cong shortening of femur	4 ins Femur	1 in	Secondary hemorrhage, infection, loss of peroneal nerve supply	4 years later Paralysis persists
S G	Polio	3 ins	2 $\frac{1}{2}$ ins	None	4 years later Fair
M B	Old epi- physitis	1 $\frac{3}{4}$ ins	1 $\frac{3}{8}$ ins	Protrusion of tibial fragment through wound	7 years later Good
P D	Polio	2 $\frac{3}{4}$ ins	2 $\frac{1}{2}$ ins	None	6 years later Good
K C	Polio	3 $\frac{1}{4}$ ins	2 ins	Slough, exposure of bone	3 years later Fair
E F	Polio	2 $\frac{1}{4}$ ins	1 in	Slough, protrusion of fragment	1 $\frac{1}{2}$ years later Fair
T L	Polio	1 $\frac{3}{4}$ ins	2 $\frac{1}{2}$ ins	Displaced epiphysis and over- lengthened leg	3 years later Good Equal length
A B	Polio	2 ins	1 $\frac{1}{2}$ ins	Nonunion Bone graft	4 years later Good
A M	Polio	3 ins	2 $\frac{3}{4}$ ins	Slight infection about pins	5 years later Result good Short leg $\frac{1}{4}$ in longer

Other common complications were nerve paralysis and muscle contracture. The nerve most frequently injured was the common peroneal, giving rise to equinovarus deformity of the foot. Foot deformity was also frequently produced by uneven tension of muscles following elongation of the bones. The rigidity of some of these contractures was so great that some basis was afforded for the view that they might be of ischemic origin.

At the Hospital for the Ruptured and Crippled, 11 operations to lengthen the tibia and fibula were performed and two to lengthen the femur (Table VI). The results were considered good in six, with an average lengthening of two inches, fair in four, poor in two and unknown in one. The most common complication after tibial lengthening was anterior protrusion of the fragments, which led to exposure of the bone in six cases. There were two cases of non-union of the tibia. Union was obtained in one, following a bone graft, but the other was complicated by bone infection, and when last seen this patient was still walking with a caliper brace.

That end-results of bone lengthening operations should not be judged too early is shown by the following case report.

Case Report—L. S., white, male, age 22, was admitted to Hospital for the Ruptured and Crippled in January, 1934, with a history of poliomyelitis at the age of one year, with resulting weakness of the right lower extremity. Examination showed flexor power of the hip weak, extensor power fair, abduction absent, quadriceps muscles poor, biceps strong, but other hamstring muscles weak, very little power in the soleus-gastrocnemius group, tibialis posterior muscle weak, the other muscles controlling the foot good. There was a four inch shortening of the right leg and an operation to lengthen the lower leg was advised.

Operation—February 1, 1934. Lengthening of tibia and fibula by the Abbott method and application of four pin extension apparatus.

Subsequent Course—The patient made a good immediate recovery. The leg was gradually lengthened and by February 26, 1934, a gain of two and one-quarter inches had been obtained, which was considered sufficient. Six weeks after operation, a small area in the operative scar broke down and discharged a small amount of seropurulent material. The drainage quickly ceased, there was good callus formation and union seemed solid. The pins were removed and a plaster encasement applied. This was changed at the end of four months, at which time some drainage from the operative area was found and there was a small piece of bone exposed in the wound. The patient was discharged to the out-patient department on crutches with the leg in plaster. This was removed January 4, 1935, and a brace fitted. The wound was still draining and bone surface was exposed. Measurement showed the left leg only three-quarters of an inch longer than the right.

The patient was readmitted May 20, 1936, for muscle transplantations of the right thigh and hip, at which time the scar over the tibia was healed and there seemed to be firm union. He was still wearing a brace but chiefly for support of the knee. The operations were performed without event in two stages on May 22, and June 12, 1936, respectively. Each was followed by immobilization of the leg in plaster for a period of two to three weeks. The patient was discharged July 21, 1936.

October 3, 1936. Patient was readmitted because of a fracture of the right tibia sustained from a fall while playing football. The upper fragment of the fibula penetrated through the skin anteriorly. The wound was cleansed and dressed and a plaster encasement applied. Discharged November 4, 1936.

January 5, 1937 Readmitted because of pseudarthrosis of the right tibia A massive onlay graft from left tibia was applied to right tibia and fixed with Sherman steel screws Progress was uneventful and he was discharged March 23, 1937, with the leg in plaster, using crutches



FIG 5—Case L. S. (A) Roentgenogram in plaster four months after lengthening operation. Two and one fourth inches of lengthening obtained. (B) View taken ten months after original operation and two months after fracture from a fall. (C) Six months after massive onlay graft for nonunion of fracture. (D) Refracture of tibia following healing of previous nonunion, four years after lengthening operation.

July 20, 1937 Readmitted because of intertrochanteric fracture of right femur sustained by a fall while walking on crutches with his leg in plaster. The grafted area of the right tibia seemed solid. A plaster spica was applied. This was removed eight weeks after injury, roentgenologic examination showed good callus formation.

EQUALIZATION OF LEG LENGTH

September 29, 1937, nine months after the bone grafting operation, the screws were removed from the right tibia as there was a small draining sinus in this area. He was discharged October 27, 1937, walking with a long caliper brace.

May 19, 1938. Readmitted because of a refracture of the right tibia sustained while turning in bed. There was still a small draining sinus. Since osteomyelitis was present and the tibia was sclerotic and thin, it was decided to amputate the leg. This was done May 25, 1938. He made a rapid recovery and was discharged.

August 15, 1938. An artificial leg was fitted and when last seen, December 10, 1938, he was walking quite well and was satisfied with his status.

SUMMARY—We feel that bone lengthening operations, although feasible, are formidable procedures and should not be undertaken lightly. They necessitate prolonged hospitalization, and are frequently followed by serious complications which may still further impair the function of an already crippled leg. Previous infection of one of the bones of the leg to be lengthened should be considered an absolute contraindication, no matter how long it appears to have been healed. Failure to observe this rule may lead to disaster. Our survey showed that lengthening operations were performed more frequently for shortening resulting from poliomyelitis than from any other condition. Yet we believe that it is precisely in such cases that the results are likely to be the most unsatisfactory. Not only are partially paralyzed muscles apt to be still further weakened by stretching but the small atrophied bones are made still smaller and more brittle by elongation. The full consequences of bone lengthening operations under these conditions are not revealed except by prolonged follow-up studies.

From our observation and experience we believe that bone lengthening operations should not be performed until growth is well established, and then only when the musculature of the leg is normal or approximately normal. In general they should be reserved for individuals of short stature who are unwilling to make any sacrifice of height by shortening of the longer leg.

Leg Shortening Operations—Shortening of the bones of the longer leg, in order to achieve equality of length, is a much older procedure than attempts to elongate the short leg by operation. Steindler credited Rizzoli with being the first to undertake this procedure. Sayre, in 1863, advocated fracturing the shaft of the femur and allowing the fragments to overlap the necessary amount. In 1908, Glaeser reported three cases in which he had performed an oblique osteotomy and obtained sufficient overlapping to overcome a discrepancy of leg length. Shands, in 1907, reported three similar cases. Brooke¹⁶ was the first to report shortening of the lower leg. He described two successful cases in 1927, in which he had removed segments of bone one and two inches long, respectively, and applied inlay grafts, obtaining solid union in four months. He also reported shortening the femur by a step-cut method, with fixation of the fragments by two beef bone screws.

Camera²¹ was the first to devise a standard method and to report any considerable series of cases. In 1933, he described his technic, which consisted of resecting a portion of the femoral shaft of the desired length, cutting this into a diamond-shaped peg, which was then used as an intramedullary graft.

to fix the fragments together. The wide portion of the diamond served to prevent the graft from penetrating too far into either fragment. He reported a series of 32 cases. As complications, he cited two cases in which the fragments separated, necessitating reoperation and insertion of a metallic suture, three postoperative infections, and two cases of delayed union. The average period of external fixation of the limb was 50 days.

Moore,⁴⁵ also in 1933, reported a series of 13 femoral shortenings. He resected sufficient bone but left a spike projecting from the distal fragment that could be shoved up into the intramedullary canal of the proximal fragment for purposes of fixation. The average amount of shortening obtained was two and one-half inches, and the average period for complete union was two and one-half months. He reported no instances of infection, malunion or nonunion.

In 1935, White⁶⁰ reported a simplified method of femoral shortening, in which he performed a transverse osteotomy of the shaft, overlapped the fragments the necessary amount and fixed them together by inserting two long pins in an oblique direction upward and inward from the lateral side. The wound was closed with the ends of the pins protruding, which were incorporated in the plaster spica encasement. The pins were removed at the end of seven weeks, and the plaster encasement at the end of eight weeks. A caliper brace was then applied, and worn until the end of four months. He reported 47 cases treated by this method, then ages varying from eight to 42 years, the majority, however, were under age 14. The average amount of shortening obtained was two and one-half inches, with a maximum of three and one-eighth and a minimum of two inches. In the younger children, he shortened one-half an inch more than was necessary, in order to allow for continued disturbance of the growth rate, and expressed the wish that he had been even more radical. He encountered infection in four cases, with seropurulent discharge about the pin wounds, all of which cleared up in less than two weeks. Two long sequestra separated from the pin wounds in another case and were extruded. Good functional results were obtained in all the cases.

At the Hospital for the Ruptured and Crippled, we have performed five femoral shortening operations according to the method of White. No complications were encountered, with the exception of one case in which pins made of a new type of steel were used and broke without, however, any loss of fixation. It was necessary to perform a later operation to remove the ends of the pins. An average shortening of two and one-eighth inches was obtained. To illustrate how much improvement in a patient's condition can be obtained by a combination of methods, the following case history is presented.

Case Report—J. H., female, age 26, was admitted to the Hospital for the Ruptured and Crippled, May 5, 1937, with a history of infection of the right hip, probably tuberculous, at age 7. This resulted in ankylosis of the hip and failure of development of the right leg, so that for years she had walked with a limp and had to wear a lift, eight

EQUALIZATION OF LEG LENGTH

inches high, under her shoe. She did not complain of any pain but was anxious to have something done to equalize the length of her legs so that she might discard her raised shoe.

Examination showed bony ankylosis of the right hip and an underdeveloped right leg. The hip was fixed in a position of 45° flexion and 15° adduction. The right knee

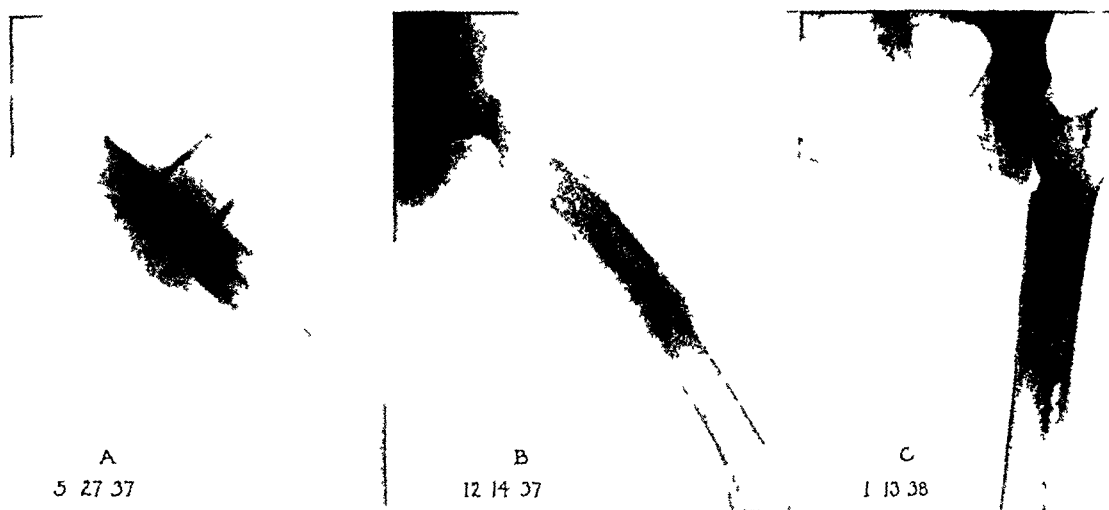


FIG 6—Case J. H. (A) Postoperative roentgenogram showing overlapping of fragments with three inches of shortening of femur and pins in place. (B) and (C) Views showing position and healing approximately eight months after operation.



FIG 7—Case J. H. (A) Preoperative appearance of patient wearing eight inch lift on shoe. (B) Appearance after three inches of shortening of left femur, correction of adduction deformity of right hip and flexion deformity of right knee by osteotomies.

showed a normal range of flexion, but extension was limited at an angle of 165° . Measurements showed the length of the right leg $28\frac{1}{2}$ inches, of the left leg $34\frac{1}{2}$ inches, of the right femur 14 inches, and of the left femur $17\frac{1}{2}$ inches. The flexed, adducted position of the right hip caused her to stand with marked lumbar lordosis.

and with the right side of the pelvis raised so that there was a relative increase of the shortening (See Figs 6 and 7)

First Operation—May 8, 1937 Shortening of left femur by oblique osteotomy, overlapping of the fragments and pin fixation Amount of shortening obtained, three inches Application of plaster spica Good postoperative recovery

Second Operation—May 24, 1937 Subtrochanteric osteotomy for correction of flexion and adduction deformity of the right hip Plaster spica applied holding hip in position of 10° abduction and 15° flexion Uneventful convalescence

Third Operation—June 21, 1937 Supracondylar osteotomy of right femur to overcome flexion deformity of right knee Bilateral plaster spica

Subsequent Course—The patient did well Union of the left femur and of the right hip appeared solid August 10, 1937, and the plaster was removed A plaster leg encasement, to support the region of the right knee, was worn until August 31, 1937 She was then given exercise treatment in the pool, and weight bearing was permitted September 15, 1937 She was discharged one week later

Patient was examined in the End-Result Clinic, October 18, 1938, at which time she stated that she was very pleased with the result She walked well with a one-quarter inch lift under her right heel The right hip was fixed in 10° abduction and 25° flexion The right knee could be completely extended and flexed to an angle of 80° The length of the legs, when measured from the anterior superior spine, was right 29 inches, left 31¼ inches, when measured from the umbilicus right 33½ inches, left 34¼ inches The abducted position of the right hip was sufficient to cause enough relative lengthening of the leg nearly to compensate for the two and three-quarters of an inch actual shortening present

SUMMARY—We feel that leg shortening operations are practical procedures, that the technic varies with different surgeons, with the preference, however, either for the resection of a portion of the shaft with fixation by an intramedullary graft or for a simple overlapping operation with fixation by pins, that the complications are few and that the functional results are good (Table VII)

TABLE VII
REPORTED RESULTS OF LEG SHORTENING OPERATIONS

Author	Number of Shortening Operations		Average Shortening Obtained	Complications Reported				Results
				Separation of Fragments Reoperation	Infections	Delayed Union	Non-union	
Brooke	1	2	1 2/3 ins	0	0	0	0	Good
Camera	32	0		2	3	2	0	Good
Moore	13	0	2 1/2 ins		0	0	0	Good
White	47	0	2 1/2 ins		4	0	0	Good
Present report	5	0	2 1/8 ins	0	0	0	0	Good
Totals	98	2	2 ins	2	7	2	0	

There is a natural prejudice, both on the part of the surgeon and of the patient, against operating upon the normal leg when the other is already

EQUALIZATION OF LEG LENGTH

crippled, but the results show that the method is justified when there is serious discrepancy in length and particularly when the shortening is three and one-eighth inches. The maximum amount of shortening reported was three and one-eighth inches, but Hey Groves stated that the normal femur might be safely shortened by 25 per cent of its total length. As far as loss of muscle power resulting from the shortening is concerned, we can confirm the statement of Hey Groves that "It is very remarkable how the full muscular power of the muscle is taken up within a few months and the leg shortening operations ought not to be performed until after growth has been well attained, both for fear that a continuing disturbed rate of growth may lead to later discrepancy in the length of the limbs and also because the resulting hyperemia may lead to an increased rate of growth on the shortened side similar to that which has been observed following fracture of the femur. Either of these factors might upset the results of equalization.

INDICATIONS FOR, AND EVALUATION OF, THE DIFFERENT METHODS FOR EQUALIZING LEG LENGTH

The purpose of the authors in preparing this report was to compare the relative merits and disadvantages of the different methods of equalizing leg length (Table VIII)

TABLE VIII

COMPARISON OF METHODS OF EQUALIZATION OF LEG LENGTH

Method	Age	Period of Hospitalization	Seriousness of Procedure	Possible Correction
Local stimulation	3-14 yrs	2 wks	+	Slight
Lumbar sympathectomy	3-10 yrs	3 wks	+++	1 in
Epiphyseal arrest	7-14 yrs	3 wks	++	4 ins
Leg lengthening	over 14 yrs	5 mos +	++++	3 ins
Leg shortening	over 15 yrs	3 mos +	+++	3 ins

CONCLUSIONS

- (1) Local stimulation of bone growth has not as yet been proved sufficiently successful to warrant clinical application
- (2) Lumbar sympathectomy, when indicated for the correction of circulatory disturbances in association with inequality of leg length, as frequently seen in poliomyelitis, may be expected to cause a favorable alteration of the diminished growth rate of the shorter extremity. Even when done before the age of nine years, improvement cannot be assured and the greatest gain that can be expected is approximately one inch
- (3) Epiphyseal arrest in comparison with the other operative methods has the advantage of being a relatively minor surgical procedure. Few, if any, complications need be anticipated. Careful calculation is necessary to determine the age at which the operation should be performed, and which

epiphyses should be fused. This depends upon the age of the patient when first seen, the amount of shortening and whether or not it is increasing. When a gross discrepancy of length is to be overcome, the operation must be performed early. Complete fusion must be obtained in order to avoid any danger of later deformity due to asymmetric growth. This method offers the simplest and safest means of equalizing leg length. Its only drawback is that its application is limited to the growing period.

(4) Leg lengthening is a formidable procedure and frequently attended by serious complications. Until these difficulties have been overcome, its use should be limited to patients who are too old for epiphyseal arrest and are unwilling or ill able to sacrifice height by undergoing shortening of the longer extremity. Previous infection of a bone of the shorter extremity is a definite contraindication. We also warn against undertaking this procedure in a severely paralyzed or atrophic extremity.

(5) Leg shortening like epiphyseal arrest, has the disadvantage that it must be undertaken on the longer and usually normal leg. It is a relatively simple and safe procedure. Serious infection, nonunion, deformity and muscle weakness have not been reported. Although the operation has been performed almost exclusively upon the femur, it has also been undertaken successfully in the lower leg. The maximum correction so far reported is approximately three inches. Leg shortening should be advised only when growth is well established. Many patients show an aversion to loss of stature, but the elimination of the raised shoe more than compensates for this. Furthermore, it should be pointed out that a lowering of the center of gravity in a patient with a crippled lower extremity usually results in a gain of stability and an improvement of locomotion. Leg shortening, therefore, has the advantage over leg lengthening, in that it actually improves function.

BIBLIOGRAPHY

- ¹ Abbott, L. C. The Operative Lengthening of the Tibia and Fibula. *J. Bone and Joint Surg.*, 9, 128, January, 1927.
- ² Abbott, L. C., and Crego, C. H. The Operative Lengthening of the Femur. *South Med J.*, 21, 823, 1928.
- ³ Abbott, L. C. The Operative Lengthening of the Tibia and Fibula. *Western J. Surg.* 39, 513, 1931.
- ⁴ Alcorn, F. A. Tibia and Fibula Lengthening by Turnbuckle Method. *Surg., Gynec. and Obstet.*, 67, 230, August, 1938.
- ⁵ Anapol, G. Leg Lengthening with Author's Technique and Apparatus. *Cir. ort. v. Traumatologia*, 6, 51, April, May, June, 1938.
- ⁶ Anderson, R. Femoral Bone Lengthening. *Am. J. Surg.*, 31, 479, March, 1936.
- ⁷ Barr, J. S., and Ober, F. R. Leg Lengthening in Adults. *J. Bone and Joint Surg.*, 15, 674, July, 1933.
- ⁸ Bergmann, E. Participation of Epiphyseal Cartilage in Growth of Long Bones. *Deutsche Ztschr. f. Chir.*, 213, 303, 1929.
- ⁹ Bergmann, E. Longitudinal Growth. *Deutsche Ztschr. f. Chir.*, 233, 149, 1931.
- ¹⁰ Bisgard, J. D. Effect of Sympathetic Ganglionectomy upon Bone Growth. *Proc. Soc. Exper. Biol. and Med.*, 29, 229, November, 1931.
- ¹¹ Bisgard, J. D. Longitudinal Bone Growth, Influence of Sympathetic Denervation. *ANNALS OF SURGERY*, 97, 374, March, 1933.

- ¹² Bisgard, J D, and Bisgard, M E Longitudinal Growth of Long Bones Arch Surg, 31, 568, October, 1935
- ¹³ Bisgard, J D, and Hunt, H B Influence of Roentgen Rays and Radium on Epiphyseal Growth of Long Bones Radiology, 26, 56, 1936
- ¹⁴ Bisgard, J D Longitudinal Overgrowth of Long Bones with Special Reference to Fractures Surg, Gynec and Obstet, 62, 823, 1936
- ¹⁵ Bohlman, H R Experiments with Foreign Materials in Region of Epiphyseal Cartilage Plate of Growing Bones to Increase Their Longitudinal Growth J Bone and Joint Surg, 11, 365, April, 1929
- ¹⁶ Brooke, J A Shortening of Bones of Leg to Correct Inequality of Length Surg, Gynec and Obstet, 44, 703, May, 1927
- ¹⁷ Brooke, R Bone Shortening for Inequality of Length in Lower Limbs Proc Roy Soc Med, 30, 441, 1937
- ¹⁸ Brooks, Bainey, and Hillstrom, H T Effect of Roentgen Rays on Bone Growth and Bone Regeneration, Experimental Study Am J Surg, 20, 599, 1933
- ¹⁹ Brockway, A Clinical Resume of 46 Leg-Lengthening Operations J Bone and Joint Surg, 17, 969, October, 1935
- ²⁰ Burdick, C G, and Siris, I E Fractures of the Femur in Children ANNALS OF SURGERY, 77, 736, 1923
- ²¹ Camera, U Surgical Shortening of Healthy Extremity in Patients with Extremities of Unequal Length, Indications, Technique and Results, 32 Cases Chir d org di movimento, 17, 569, February, 1933
- ²² Carrell, W B Leg Lengthening South Med J, 22, 216, March, 1929
- ²³ Chandler, F A Local Overgrowth J A M A, 109, 1411, 1937
- ²⁴ Cole, W H Leg Lengthening for Shortening Due to Infantile Paralysis Minnesota Med, 13, 904, December, 1930
- ²⁵ Compere, E L Growth Arrest in Long Bones as a Result of Fractures That Include Epiphyses J A M A, 105, 2140, 1935
- ²⁶ Compere, E L Indications For and Against Leg Lengthening Operation, Use of Tibial Bone Graft as Factor in Preventing Delayed Union, Non-union or Late Fracture J Bone and Joint Surg, 18, 692, July, 1936
- ²⁷ Compere, E L, and Adams, C O Studies of Longitudinal Growth of Long Bones, Influence of Trauma to Diaphyses J Bone and Joint Surg, 19, 922, October, 1937
- ²⁸ Dahl, B Effect of Roentgen Ray on Developing Long Bones, Roentgenographic and Anatomic Study J de Radiol et d'elect, 18, 131, 1934
- ²⁹ Dickson, F D, and Diveley, R L A New Apparatus for the Lengthening of Legs J Bone and Joint Surg, 14, 194, 1932
- ³⁰ Digby, K H The Measurement of Diaphyseal Growth in Proximal and Distal Directions J Anat and Physiol, 50, 187, 1915-1916
- ³¹ Ferguson, A B Surgical Stimulation of Bone Growth by New Procedure, Preliminary Report J A M A, 100, 26, 1933
- ³² Gatewood and Mullen Experimental Observations on Growth of Long Bones Arch Surg, 15, 215, August, 1927
- ³³ Groves, E W Hey An Address on Stature and Poise The Problem of Unequal Legs Brit Med J, 2, 1, 1931
- ³⁴ Haboush, E J, and Finkelstein, H Leg Lengthening with New Stabilizing Apparatus J Bone and Joint Surg, 14, 807, October, 1932
- ³⁵ Harris, R I The Effect of Lumbar Sympathectomy on the Growth of Legs Shortened from Anterior Poliomyelitis, a Preliminary Report J Bone and Joint Surg, 12, 859, 1930
- ³⁶ Harris, R I, and McDonald, J L The Effect of Lumbar Sympathectomy upon the Growth of Legs Paralyzed by Anterior Poliomyelitis J Bone and Joint Surg, 18, 35, 1936

- ³⁷ Horton, B T Hemihypertrophy of Extremities Associated with Congenital Arterio-venous Fistula J A M A , 98, 373, 1932
- ³⁸ Janes, E C Experiences in Leg Lengthening J A M A , 105, 1419, November 2, 1935
- ³⁹ Johnston, R A Y Effect of Inflammation on Epiphyses Arch Surg , 32, 810, 1936
- ⁴⁰ Kishikawa, E Studien uber einige lokale reize, welche das langengewachstum des langrohrenknochens steigern Fukuoka Acta Med (Abstract Section), 29, 4, 1936
- ⁴¹ Levander, G Increased Growth of Long Bones of Lower Extremities after They Have Been Fractured Acta Chir Scandinav (Supp 12), 65, 5-237, 1929
- ⁴² Magnuson, P B Lengthening Shortened Bones of the Leg by Operation Surg , Gynec and Obstet , 17, 63, 1913
- ⁴³ Meisenbach, R O A Consideration of the Chemical and Mechanical Stimulation of Bone with Reference to the Epiphyseal and Diaphyseal Lines, Results of Animal Experimentation Am J Orthop Surg , 8, 28, 1910
- ⁴⁴ Moore, B H A Bone Lengthening Apparatus J Bone and Joint Surg , 13, 170, 1931
- ⁴⁵ Moore, J R Tibial Lengthening and Femoral Shortening Pennsylvania M J , 36, 751, July, 1933
- ⁴⁶ Ollier, L Traite experimental et clinique de la regeneration des os et de la production artificielle du tissu osseux Paris, Tome 1, Masson et fils, 1867
- ⁴⁷ Peabody, C W Hemihypertrophy and Hemiatrophy J Bone and Joint Surg , 18, 466, 1936
- ⁴⁸ Perthes, G Uber den Einfluss der Rontgensstrahlen auf Epitheliale Gebilde Insbesondere auf das Carcinom, Arch f klin Chir , 71, 955, 1903
- ⁴⁹ Phemister, D B Operative Arrestment of Longitudinal Growth of Bones in Treatment of Deformities J Bone and Joint Surg , 15, 1, 1933
- ⁵⁰ Pitzen, P Experiments to Promote Longitudinal Growth of Long Bones Ztschr f orthop Chir , 49, 554, 1928
- ⁵¹ Putti, V The Operative Lengthening of the Femur J A M A , 77, 934, 1921
- ⁵² Putti, V Operative Lengthening of the Femur Surg , Gynec and Obstet , 58, 318, February, 1934
- ⁵³ Speed, K Longitudinal Overgrowth of Long Bones Surg , Gynec and Obstet , 36, 787, 1923
- ⁵⁴ Stephenson, J B, and Durham, H A End-results in Leg Lengthening South Med J , 28, 818, September, 1935
- ⁵⁵ Stewart, S F Effect of Sympathectomy on the Leg Length in Cortical Rigidity J Bone and Joint Surg , 19, 222, January, 1937
- ⁵⁶ Snyder, C H Deformities Resulting from Unilateral Surgical Trauma to the Epiphyses ANNALS OF SURGERY, 100, 335, 1934
- ⁵⁷ Truesdell, E D Inequality of the Lower Extremities Following Fracture of the Shaft of the Femur in Children ANNALS OF SURGERY, 74, 498, 1921
- ⁵⁸ Warwick, T W, and Wiles, P Growth of Periosteum in Long Bones Brit J Surg , 22, 169, 1934
- ⁵⁹ White, J W Simplified Method for Tibial Lengthening J Bone and Joint Surg , 12, 90, January, 1930
- ⁶⁰ White, J W Femoral Shortening for Equalization of Leg Length J Bone and Joint Surg , 17, 597, July, 1935
- ⁶¹ White, J W, and Warner, W P, Jr Experiences with Metaphyseal Growth Arrests (Technique for Shortening Leg), 59 Cases South Med J , 31, 411, April, 1938
- ⁶² Wu, Y K, and Miltner, L J Procedure for Stimulation of Longitudinal Growth of Bone—Experimental Study J Bone and Joint Surg , 19, 909, October, 1937

DISCUSSION—DR CLAY RAY MURRAY (New York) said that Doctor Wilson and Doctor Thompson had presented one of the very best surveys of a difficult problem he had ever listened to. One of the most important features of the paper is that it did not stress so much the operative procedure

as the evaluation that every one of the cases presented had been put through before any operative procedure was attempted. Studies of the development of the child's background, familial growth, the particular stage of growth the child happened to be in (the very active growth that children go through, or one of the latent periods)—all were carefully evaluated before either operative procedure was undertaken or before the time for such procedure was chosen. Even if a method is ideally carried out, and despite the method used, without extremely careful and prolonged evaluation before carrying it out, its value may be very largely lost.

DR ALAN DE FOREST SMITH (New York) said that he had come to the same conclusions at the N. Y. Orthopedic Hospital as had Doctor Wilson, in evaluating the various methods of dealing with disturbance in the length of extremities. Leg lengthening is a very difficult and dangerous procedure, and fraught with many risks. It is reserved at the N. Y. Orthopedic Hospital for the very few cases in which the discrepancy is so great that it is impossible to overcome it by leg shortening.

Leg shortening is preferred in most cases by epiphyseodesis in young children, before the end of their growth period, and by taking some bone out of the femur in adults and older children. Before dealing with this problem with entire success, it is necessary to have more data on the behavior of growth especially in poliomyelitis cases. Not enough is known about the effect of poliomyelitis on growth. From cases observed by Doctor Smith it is his opinion that they reach a stationary point at which there is no longer an inequality in rate, before the end of their growth period. A discrepancy in the growth of the extremities may result so that an extremity may lose an inch or two during a certain period of time. This difference then remains until the end of growth. If the behavior of these cases was more fully understood one would be better able to deal with them.

CLINICAL AND EXPERIMENTAL EXPERIENCES IN THE SURGICAL TREATMENT OF HYPERTENSION*

LOYAL DAVIS, M D , AND M HERBERT BARKER, M D

CHICAGO, ILL

FROM THE DIVISIONS OF SURGERY AND MEDICINE, NORTHWESTERN UNIVERSITY MEDICAL SCHOOL, CHICAGO, ILL

IN 1935, one of us¹ (M H B) reported his clinical experiences with and the mode of action of the sulphocyanates in the treatment of hypertension. It was found that if the oral dosage was adjusted until the cyanate content of the blood ranged between 6 and 12 mg per 100 cc , a reduction of the blood pressure occurred in 35 of 45 patients with systolic blood pressures well over 200 Mm of mercury. The blood pressure reduction was well maintained for months and even years in the individuals sensitive to this drug, if an average concentration of 10 mg per 100 cc of blood was held. It was emphasized that the dosage necessary to maintain a therapeutic concentration of the cyanates in the blood varies greatly, apparently due to the individual sensitivity and clearance of the mineral from the body. Since then, experience with a larger group of patients has been obtained, and these results have been corroborated^{2 3}

The most striking effect produced by the cyanates is the drop of the systolic blood pressure. Decreases from 270 or 220 Mm down to levels between 180 and 140 Mm have been frequently produced and although the diastolic pressure usually lags some days or weeks, a reduction to levels of 80 to 100 Mm may be obtained. The cardiac symptoms of heart consciousness, shortness of breath and nocturnal dyspnea usually decrease as the blood pressure falls and relief from headache, insomnia and nervousness often occurs even without the expected proportionate decrease in blood pressure. Compensation of the heart has generally followed, and is easily maintained, as long as the reduction of the blood pressure is held. A decrease of the size of the heart takes place in a few weeks, as may be shown by orthodiagrams and two meter roentgenograms. No damage to the concentration power of the kidneys nor retention of waste products has been encountered as the blood pressure has been reduced. At the same time, a fairly regular decrease in the red cell count, hematocrit, blood cholesterol and the total serum proteins has been observed if the cyanate therapy is continued and a proper blood cyanate level is held. The sedimentation rate is increased and there is an ease in drawing blood through a standard caliber needle, which suggests that the total blood viscosity is materially reduced.

In a series of over 200 cases, roughly 50 per cent have shown symptomatic improvement, with blood pressure reductions that are regarded as significant and satisfactory responses following cyanate therapy. In 25 per cent, an

* Read before the American Surgical Association, Hot Springs, Va , May 11, 12, 13, 1939

escape from the therapeutic effects of the drug occurs after a good initial response. In these latter patients, there is an enormous augmentation of the clearance of the drug, so that very much larger doses are required to maintain a satisfactory blood cyanate level. In the remainder, a gradual rise in blood pressure occurs in the face of a constantly maintained and seemingly adequate blood cyanate concentration, large enough in many instances to produce toxic symptoms. Of all the patients in this latter group, 50 per cent may be regarded as resistant to cyanate therapy.

For this group of cyanate resistant patients with hypertension, we have considered the possible advantages of surgical therapy. In a previous paper⁴ we presented our criteria for choosing patients for the operation of bilateral supradiaphragmatic splanchnicectomy and set down the studies and observations which we carried out on each patient pre- and postoperatively.

(1) All patients have a severe grade of essential hypertension with a systolic pressure of 200 Mm or over and with a diastolic pressure above 100 Mm of mercury. (2) As far as can be detected by a careful history, physical examination and laboratory data, there is no evidence of chronic glomerular renal disease. (3) There is no evidence of significant peripheral arterial sclerosis. (4) Throughout their months or years of observations, blood pressures show normal fluctuations, that is, the pressures are not "frozen" at a definite level. (5) All of the patients have been given a thorough trial with potassium sulphocyanate over a period of several months up to two years. The sulphocyanates have been discontinued for one of two reasons, either the patient shows some response to cyanate therapy but the dose necessary to lower his blood pressure is large enough to cause symptoms of sulphocyanate intoxication, or he is not sensitive to the drug, particularly in regard to his diastolic blood pressure.

Briefly, then, relatively young hypertensive patients without renal damage whose blood pressures under normal conditions show rather marked fluctuations, whose vascular tree is still elastic, and who, over a long period of time for one of two reasons, have been found to be insensitive to potassium sulphocyanate therapy are subjected to critical study and observation before and after operation. These studies and observations consist of

(1) Renal function tests of concentration and dilution power, urea clearance and fractional phenolsulphonphthalein excretion.

(2) Blood chemistry studies which include total serum protein, serum albumin and globulin, cholesterol, uric acid, blood and fluid volume, hematocrit, chlorides, CO₂ capacity, urea nitrogen, glucose and insulin tolerance.

(3) Blood pressures are taken morning and evening, during bed rest, for a period of four days and continued until a normal basal level has been reached. Blood pressure readings are then made while the patient is ambulatory, after meals, during periods of nervousness or excitement, and while asleep.

(4) The cold pressor test done according to the method described by Hines and Brown.

(5) A tablet of nitroglycerine (1/200 to 1/100 gr) is placed under the tongue, and the drop in the pressure is recorded for a 20-minute period, or until the readings show that the pressure has returned to the average normal level

(6) Changes in the blood pressure during a period of deep sleep induced by amytal, pentothal of sodium and aveitin are recorded

(7) Carbon dioxide inhalations are given to determine how high the blood pressure may be elevated under controlled conditions

Clinical Experiences—Recognizing from the outset that by limiting our choice of patients to those who had been proven to be cyanate resistant we necessarily were choosing difficult cases upon which to test the effect of a surgical procedure, we still were not quite prepared to meet the complete failures which attended our efforts in the first three patients operated upon

Case 1—D G, female, age 29, was first aware that she had hypertension at age 24, in 1930. By 1932, she had edema of the ankles and had begun to tire easily at her work. The following year, she was forced to leave her position and was admitted to the Cardiovascular Clinic, complaining of severe headaches, dizziness, dyspnea, precordial pain, palpitation, insomnia and nocturia

The blood pressure was 220/130 Mm. The heart was of normal size with only a moderately forceful apex impulse. The apical tones were muffled and there was a harsh rasping murmur occupying all of systole and diastole heard at the root of the neck on the right. The blood urea nitrogen was 13.4 mg, cholesterol 235 mg, blood chlorides 480 mg and the phenolsulphonphthalein excretion test totalled 60 per cent in two hours. The left optic fundus showed edematous tissue about the vessels near the disk.

The patient was given 0.3 Gm of potassium sulphocyanate twice daily and this dosage was gradually increased to learn her tolerance. During the next year she was out of the city at intervals and the blood cyanate level was difficult to control, but at no time did it ever exceed 6.9 mg per 100 cc of blood. Some of her symptoms were reduced, but none disappeared, and her blood pressure ranged near 220/100 Mm. From April, 1935, to July 1, 1935, the blood cyanate level was gradually raised to 19.3 mg, but her headaches, dizziness, dyspnea and other symptoms continued unchanged.

She was placed in the hospital and kept in bed for two weeks without cyanate therapy. Her blood pressure remained unchanged and her symptoms continued with even greater intensity. When her blood had become entirely free from cyanates her hematocrit reading was 41 per cent, total proteins 8.14 Gm, albumin 4.95 Gm, globulin 2.49 Gm, urea nitrogen 13.5 mg, uric acid 2.5 mg, cholesterol 231 mg, urea clearance 46 per cent, chlorides 440 mg with a carbon dioxide capacity of 50.5 per cent.

On July 12, 1935, a bilateral supradiaphragmatic splanchnicectomy was performed and there was an immediate postoperative drop in the blood pressure to 154/90 Mm, but this lasted only three hours and quickly rose within seven hours to 180/114 Mm. An insulin tolerance test was performed several weeks later, and the patient had a violent hyperinsulin reaction after the injection of 10 units of insulin, quite characteristic of the reaction following section of the splanchnic nerve.

The patient's blood chemistry findings showed no essential change whatever upon several postoperative examinations, and although cyanates have been given at various intervals during the past three years following operation the blood pressure levels have never been critically lowered.

Quite convinced of the completeness of the operative procedure, we could only conclude that we had chosen a patient whose blood pressure levels

were frozen. We had not subjected this patient to any of the tests employed at other clinics in an effort to choose patients who might be expected to react favorably to an interruption of the splanchnic nerves. This, we believed, was an oversight which might have prevented us from subjecting the surgical procedure to a test far beyond its scope and so we approached the second case hoping that a favorable response to various tests for vascular lability might carry a more hopeful prognosis.

Case 2—R. K. V. was refused an insurance policy in 1931, at the age of 34, because of a systolic blood pressure of 240 Mm. From 1933 until the fall of 1936, the patient was under medical management elsewhere, which succeeded in keeping his systolic pressure in the neighborhood of 150 Mm. He continued his work as a newspaper man and felt well. In October, 1936, he had bleeding from his left kidney and during hospitalization at that time his pressure had again risen to a systolic level of 240 Mm. From that time, to the time of his entrance into our clinic, he had complained of dyspnea, blurring of vision, severe headaches, precordial pain and a constant hematuria.

Upon examination February 13, 1937, the patient had a blood pressure of 266/166 Mm, his fundi showed a bilateral papilledema with tortuous retinal arteries, hemorrhages and exudates. There was no cardiac enlargement but the peripheral vessels were tortuous and the pulse was bounding and not easily compressed. A cold pressor test and the nitroglycerine test caused no significant change in his blood pressure levels. Pentothal sodium (1 Gm.) was injected intravenously and although the systolic pressure fell while the patient was asleep it was not a marked change. During three weeks of absolute bed rest during which time potassium sulphocyanate was administered until the blood level was 127 mg. per 100 cc., there was no change in his blood pressure and his symptoms remained unchanged.

Previous to the administration of cyanates the patient's hematocrit reading was 41 per cent, blood urea nitrogen 19.4 mg., cholesterol 368 mg., chlorides 448 mg., urea clearance 55.5 per cent, total protein 8.08 Gm., albumin 3.06 Gm., and the carbon dioxide capacity 60.4 per cent. After the administration of the cyanates the hematocrit reading decreased to 39 per cent and the other blood chemistry determinations were essentially unchanged.

On March 22, 1937, a bilateral supradiaphragmatic splanchnicectomy was performed and although the immediate postoperative blood pressure was 154/110 Mm, within 24 hours it had risen to 195/130 Mm and never fell below that level until his discharge on April 18, 1937, when it was 210/135 Mm. Again, an insulin injection of 10 units produced a typical shock reaction in this patient.

The patient's symptoms continued unchanged and there was no significant change in any of the blood chemistry determinations. The phenolsulphonphthalein excretion test was 64 per cent in two hours, practically the same as it was prior to operation, and the urea clearance test was not significantly altered.

The patient was discharged under the care of his own physician and succumbed within three months as the result of a cerebral vascular accident. During this time he had not been given sulphocyanates.

This second experience was even more discouraging than the results obtained in the first patient. Although his responses to the cold pressor, nitroglycerine and pentothal tests indicated a nonlabile vascular system, we felt that in view of the malignancy of his disease and his hopeless outlook, and our inability to place complete reliance upon the tests for vasomotor lability, he should be given the benefit of whatever advantages an operation might afford him. Thus far, in two patients we had not adhered to the

principles we had established for surgical indications and, in partial extenuation, had been unduly influenced by favorable reports in the literature. We were unable to satisfy ourselves that our cases were comparable in their clinical manifestations.

Certainly no changes had occurred in the various constituents of the blood. Likewise neither patient showed any improvement whatever in the subjective symptoms nor was there a change in the fundus findings following operation, both of which had been reported as a rather constant occurrence, irrespective of the effect upon the blood pressure.

We persisted in looking for a patient with severe hypertension, resistant to cyanate therapy, whose reactions to vasoconstrictor and vasodilator tests might give us encouragement. Finally, we believed that we had found one who might prove to be a less difficult problem, for, although she was resistant to the administration of cyanates, she exhibited prompt and marked reactions to the cold pressor, nitroglycerine and sodium pentothal tests.

Case 3—F M, female, age 38, was first aware of a hypertension in 1933, when she was age 34. She had suffered during the following four years with severe headaches, dyspnea, indigestion, fatigue, backache, and pain in her chest. Her blood pressure was 260/160 Mm, the peripheral vessels were firm and there was a slight edema over the tibiae. The heart was enlarged to the left, the rhythm was regular and the tones were of moderate intensity with a systolic murmur at the apex and base. The optic disk margins were blurred bilaterally, the retinal vessels were small and there was a slight edema of the retinae.

The patient's blood pressure upon rest in bed was 182/108 Mm and ten minutes after immersing her right arm in water at 40°C for half a minute it had risen to 208/118 Mm. Two minutes after taking 1/100 gr of nitroglycerine the pressure had decreased from 204/118 to 176/114 Mm, six minutes later it had returned to 180/118 Mm. She felt after this test as if "all the blood was rushing to her head" and 15 minutes later complained of a terrific headache. Two minutes after starting the injection of 2 Gm of sodium pentothal, her blood pressure dropped from 230/135 to 165/120 Mm. The injection was continued slowly for 15 minutes, during which the patient remained asleep and the blood pressure lowered. Thirty minutes after the injection had stopped the blood pressure had returned to 210/120 Mm.

On March 17, 1937, a bilateral supradiaphragmatic splanchnicectomy was performed, and a drop in the blood pressure was present for 12 hours immediately postoperative. Since that time, it has remained in the vicinity of the preoperative level although the patient's dyspnea and sense of chest constriction are greatly improved. The sodium pentothal test following operation showed a response exactly similar to that found before operation, as did the other tests for vascular lability.

This, then, was the third unsuccessful result we had encountered after sectioning the splanchnic nerves supradiaphragmatically. We had found no lead in a study of the blood chemistry before and after operation in two patients and finally we had been misled by responses to tests for vascular lability. Although all of these patients presented severe cases of essential hypertension and perhaps should never have been candidates for surgery because of the stage of their disease, we believed that similar patients had been operated upon elsewhere with an immediate drop in the blood pressure which had remained permanently lowered. Our only conclusions could be that either the operation

HYPERTENSION

was ineffective or that we had chosen patients in whom the state of the disease was so far advanced that the operation should not have been expected to have been of help and that these patients were in no way comparable to those operated upon elsewhere.

During this period, Goldblatt and others had reported the production of hypertension experimentally in dogs, and had shown that even a total sympathectomy did not influence the hypertension which followed partial occlusion of the renal arteries. Although many operations had been performed upon patients, no physiologic explanation had been forthcoming to account for the clinical improvement observed in other clinics.

At this point, when we were convinced that the problem should be attacked from several angles in the experimental laboratory before we attempted the operation again in patients, we had an experience with a patient who had been under the care of one of us (M H B) for many months. This individual (M₁ C C G), age 39, presented all of the symptoms of a severe, essential hypertension with a systolic blood pressure ranging from 200 to 260 Mm and a diastolic pressure of 120 to 140 Mm. He had been placed upon cyanate, and his blood cyanate level had been maintained for a number of weeks well above the average of 10 mg per 100 cc of blood, without any effect whatever upon his symptoms or blood pressure levels.

He had visited the Mayo Clinic in March, 1936, where his blood pressure was found to be 260/140 Mm. He had gone to that Clinic as a candidate for surgical treatment, but his responses to the tests employed there were such that he was not considered a suitable patient for operation. He returned to Chicago, and somewhat in desperation was again given cyanates, but this time his blood cyanate level was gradually raised to 20 mg per 100 cc of blood. Much to our surprise, his symptoms greatly improved and his blood pressure level was reduced to levels between 135 and 160 Mm systolic and 100 and 120 Mm diastolic. Mentally depressed, tired, and weak, he again returned to The Mayo Clinic where examination confirmed our impression that he was greatly improved except for the symptoms which could be ascribed to toxicity due to potassium sulphocyanate.

At this time (January 21, 1938), he was considered a suitable patient for operation and an infradiaphragmatic section of the splanchnic nerves, removal of the lumbar sympathetic ganglia, and a partial removal of the adrenal glands were performed. During his stay at The Mayo Clinic (until March 17, 1938) the lowest postoperative blood pressure reading was 150/110 Mm. By May, 1938, when he had returned to Chicago, however, his blood pressure had risen to 240/130 Mm, all of his previous symptoms had returned and signs of cardiac decompensation were present. Again cyanates were administered and again, to our surprise, his blood pressure was maintained at a level below 160/120 Mm on a blood cyanate level of only 10 mg per 100 cc or less (Chart 1).

In other words, the patient had become sensitive to potassium sulphocyanate and he was clearing the drug efficiently, whereas prior to operation

he had been resistant and higher blood cyanate levels with the accompanying symptoms of mild cyanate intoxication had been necessary to reduce his blood pressure. Accompanying this reduction in blood pressure there had been a marked improvement in the patient's symptoms so that he was able to resume his former social and economic position, and there had been a definite improvement in his blood chemistry findings, evidenced by a drop in his blood cholesterol, total proteins and hematocrit readings.

Now, more than a year after operation, his blood pressure level is 175/100 Mm with a blood sulphocyanate level of 12 to 14 mg, his symptoms remain improved and he is at work.

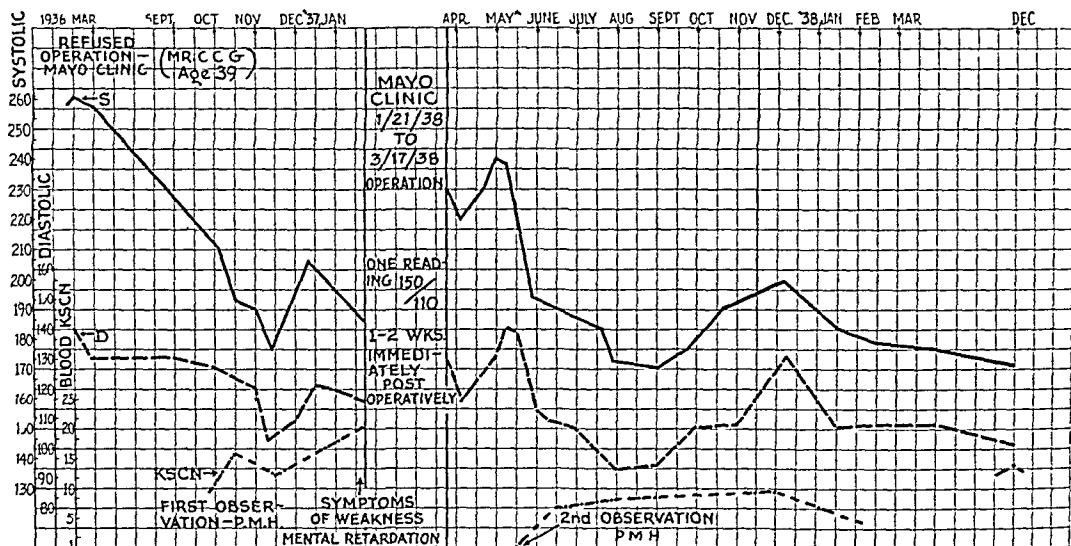


CHART 1—Graph which shows the course of the blood pressure readings and the blood cyanate levels in patient C C G before and following operation. Note also the blood pressure readings with the lower cyanate levels following operation.

We were quite unable to explain, physiologically, this improvement in the patient's ability to clear sulphocyanate more efficiently from his blood stream and to obtain the improved results from this drug. Nevertheless, it provided the encouraging stimulus to attack the problem anew both in the experimental laboratory and upon similar sulphocyanate resistant patients.

Our next patient was a schoolmistress whose hypertension, usually in the neighborhood of 200/130 Mm, was first noted in 1934, when she came under observation with the complaint that she had had frequent colds which kept her from her work.

Case 4—E M., female, age 32, was found to have a streptococcic infection of her nasopharynx. This was successfully treated, but in spite of a general improvement in her health she continued to complain of palpitation, throbbing of the vessels in her neck, attacks of dyspnea, occasional attacks of precordial pain, edema of the ankles and severe headaches. The cardiac borders were slightly enlarged to the left and the tones were accentuated but no murmur was present. There were no signs of decompensation. The optic fundi showed small retinal arteries, with thickened walls, blurred nasal borders of the optic nerve heads but no edema of the retinae.

The patient was placed upon sulphocyanate therapy, and it was found that if she remained in bed, her blood pressure could be reduced to 150/102 Mm but upon resump-

tion of her normal duties the systolic and diastolic pressures immediately rose to levels of 200 and 130 Mm, respectively, and all of her symptoms returned. Pushing the sulphocyanate therapy to high levels, at which symptoms of weakness and mental retardation were present, failed to improve her condition as long as she attempted to maintain her economic position.

On June 29, 1937, a cold pressor test was performed. Placing the left arm in water at 32°C increased the blood pressure from 176/132 to 200/136 Mm in four minutes.

Nitroglycerine (1/100 gr) beneath the tongue reduced the blood pressure from 192/134 to 172/130 Mm in four minutes, accompanied by a bounding pulse, increase in the respirations and a sensation of weakness. Eighteen minutes after the nitroglycerine was given, the pressure level was 162/128 Mm. The blood pressure had returned to its former level at the end of 35 minutes.

One Gm of sodium pentothal was injected slowly with the blood pressure level at 182/130 Mm. The lowest point reached by the blood pressure during her sleep was 152/110 Mm.

On July 1, 1937, the hematocrit reading was 43 per cent, urea nitrogen 15 mg, uric acid 2.86 per cent, cholesterol 236 mg, urea clearance 39.6 cc or 73.2 per cent, total proteins 6.80 Gm. Ten units of insulin reduced the blood sugar from 85.2 to 63.0 mg in three hours. The phenolsulphonphthalein test was 65 per cent.

On August 26, 1937, a bilateral supradiaphragmatic splanchnicectomy was performed, and although there was an immediate postoperative drop in the blood pressure levels, the preoperative state was reached within four days and remained so elevated until the time of her discharge September 20, 1938, when it was 180/130 Mm.

The cold pressor test was repeated September 17, 1937, and the pressure rose from 170/134 to 194/144 Mm. The nitroglycerine test was followed by a fall in the blood pressure levels from 180/134 to 168/128 Mm. At this time, ten units of insulin reduced the blood sugar fasting level from 39.0 mg, so that within an hour there was not enough sugar in the blood to be tested.

The blood chemistry determinations January 6, 1939, a year and one-half after her operation, showed a hematocrit reading of 40 per cent, total proteins 7.42 Gm, cholesterol 258 mg, chlorides 520 mg, carbon dioxide capacity 50.4 per cent, urea clearance 67.1 per cent, blood urea nitrogen 17.2 mg, phenolsulphonphthalein 40 per cent in 15 minutes. The cold pressor test showed a rise in blood pressure of 138/94 to 158/118 Mm. The nitroglycerine test produced no change whatever in the systolic or diastolic pressures. The sodium pentothal test showed a drop in the pressure from 138/94 to 110/80 Mm, and the carbon dioxide test showed a rise from 134/96 to 186/158 Mm.

Chart 2 shows the charted course of her blood pressure readings since September 12, 1934. Sulphocyanate therapy quickly produced a fall in the blood pressure, particularly when the patient was at rest, but when the blood was free from sulphocyanate the pressure rapidly rose. It was also noted that the blood sulphocyanate had to be raised to a higher level to effect the same result upon the blood pressure when she was at her work. Following splanchnicectomy her blood pressure is maintained at a constantly lower level upon small doses of potassium sulphocyanate while she is carrying on her normal daily duties, with blood sulphocyanate levels comparable to those which maintained the pressure at those levels when she was at bed rest prior to operation.

This patient afforded a confirmation of what we had suspected had occurred in the former patient. Observed as she was for three years before operation, during which time she had received cyanate therapy her blood chemistry findings were more nearly normal than any of the patients we had studied previously. Her cholesterol was low and her hematocrit reading was fairly normal. On the other hand, her total blood proteins were elevated and her dye excretion and urea clearance tests were not the best. In other words,

one might argue that she was a more favorable patient for operation, if one did not remember that, although she responded to sulphocyanate therapy, it was only when she restricted her activities. The problem then was a practical one of attempting to make this patient economically independent. This has been accomplished by cyanate administration after splanchicectomy, and during the past 18 months she has carried on her full duties as a teacher, by which she supports her mother and has done extra work in music, with a satisfactory blood pressure level. The patient's objective symptoms have all disappeared and recur only when she stops taking potassium sulphocyanate, as we have asked her to do several times to observe the subsequent rise in blood pressure.

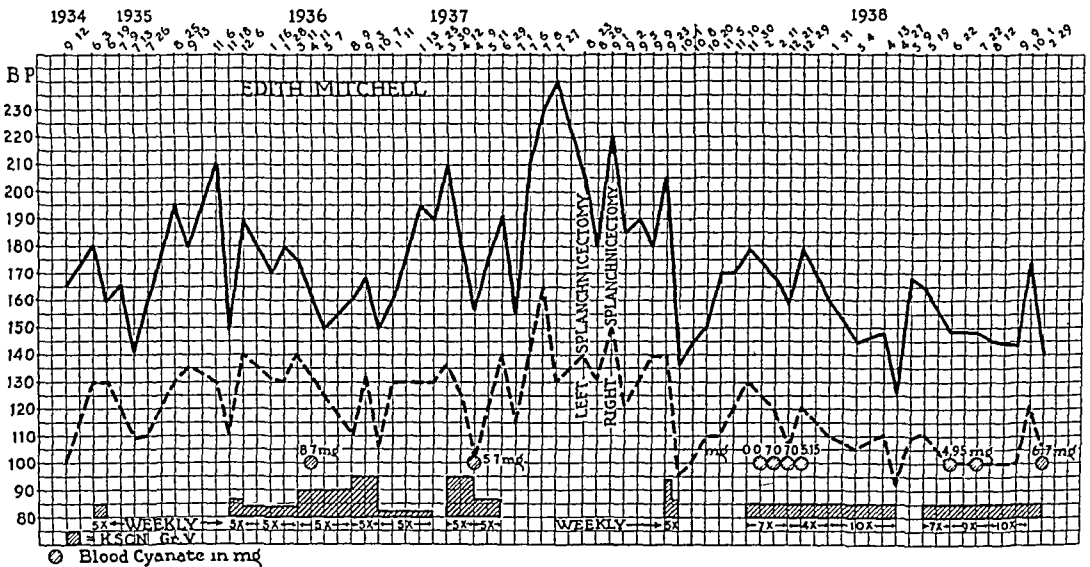


CHART 2—Graph which shows the blood pressure readings and blood cyanate levels in patient E M from 1934 to January 1939. The patient's blood pressure is definitely more responsive to smaller concentrations of cyanate in the blood following splanchnicectomy.

The excellent response of this patient stimulated us to investigate this particular phase of the problem further in other patients. As a result, we have centered all of our attention, clinically and experimentally, upon a specific phase of the surgical problem of hypertension, because in our hands, at least, it has been the only hopeful avenue of approach to the question.

The next patient was chosen for surgical treatment because, to our minds, he presented a difficult test to which we might put the idea that after splanch-
nicectomy the hypertensive patient would react more satisfactorily to the
administration of potassium sulphocyanate. We had not been able to decide,
from the observations made, whether or not less sulphocyanate was actually
required to keep the blood pressure at a lower level or whether the drug pro-
duced its effect and was more rapidly cleared from the blood stream.

Case 5—C R, male, age 25, when first seen by one of us (M H B), was in a deep coma and was having a series of convulsive seizures. He had been known to have a high blood pressure in 1931, and until December, 1935, had continued about his school duties although he complained of constant severe headaches. In February, 1936, he was taken to a hospital in coma, with severe vomiting and repeated convulsions. Potassium sulphocyanate was given intravenously with immediate cessation of the convulsions, re-

turn to consciousness and a decrease in his blood pressure levels from 260/160 to 170/120 Mm. This level was maintained successfully for 18 months, though toxic symptoms were present from time to time and close attention to the administration of the sulphocyanate was necessary.

Prior to consideration of a splanchicectomy, the drug was stopped and his pressure rose while in the hospital to 230/150 Mm. The cold pressor test showed no change in the blood pressure level. On January 4, 1938, the hematocrit reading was 37 per cent, urea nitrogen 25 mg, uric acid 4.15 mg, cholesterol 260 mg, chlorides 496 mg, carbon dioxide capacity 55.3 per cent, total protein 5.58 Gm, albumin 3.80 Gm and globulin 1.78 Gm. The phenolsulphonphthalein test showed an excretion of 50 per cent of the dye.

On January 10, 1938, a left supradiaphragmatic splanchicectomy was performed. The blood pressure dropped for a few hours after the operation but within 12 hours was 212/150 Mm.

On January 22, 1938, the patient began to complain of headache and dimness of vision. His blood pressure was 244/170 Mm. He soon became comatose and began to have a series of convulsive seizures, a clinical picture exactly similar to his condition in 1936. He was again given potassium sulphocyanate intravenously and in addition magnesium sulphate. His convulsions ceased, he became conscious and by January 25, his blood cyanate level was 4.25 mg. At that time, there was a bilateral edema of the optic disks but no marked engorgement of the retinal veins and there were no retinal hemorrhages.

It was decided that we could never free him from the drug because of the danger involved and consequently he was kept on sulphocyanate therapy until we sectioned the right splanchic nerve on February 14, 1938.

Upon discharge from the hospital March 4, 1938, the hematocrit reading was 31 per cent, urea nitrogen 21.4 mg, uric acid 2.0 mg, cholesterol 240 mg, chlorides 472 mg, carbon dioxide capacity 70.5 per cent, urea clearance 48 per cent and the blood cyanate level was 11.8 mg.

The patient has been upon sulphocyanate therapy since, with a blood pressure level ranging around 170/110 Mm, free from symptoms and physically active. On January 17, 1939, the hematocrit reading was 27 per cent, total proteins 5.71 Gm, albumin 4.16 Gm, globulin 1.55 Gm, nonprotein nitrogen 48.5 mg, blood urea nitrogen 34.9 mg, uric acid 3.76 mg, calcium 8.24 mg, phosphorus 3.12 mg, cholesterol 212 mg, chlorides 552 mg, carbon dioxide capacity 55.3 per cent, urea clearance 63.2 mg, or 84 per cent, and blood cyanates 26.6 mg. He has been carefully followed now for one year following his operation and his improvement remains while he follows a normal active life (Chart 3).

The necessity for keeping this patient upon potassium sulphocyanate therapy during the time we were attempting to determine the effect of splanchicectomy made it impossible to draw any conclusions from the blood chemistry findings or other tests after the operation. During this past year, following splanchicectomy, the patient has shown an increased sensitivity to sulphocyanate and although his blood cyanate level must be kept at a comparatively high concentration his reactions to the drug have been less and his condition therefore far more satisfactory. It would be difficult to attribute this change in the patient's response to the drug to some unknown factor inherent in the course of his disease and we believe that it can more logically be said to follow section of his splanchic nerves.

The last patient to whom we wish to direct attention in this communication, has shown the same excellent response recorded in the patient E. M.

(Case 4) Most striking, has been the manner in which the total proteins in the blood, and particularly the globulin fraction, have fallen after her operation. Previous to operation, though a high level of blood cyanate concentration was reached without the production of toxic symptoms, neither her blood pressure levels nor her blood chemistry findings showed any of the changes so characteristic of the results obtained in patients who respond favorably to cyanate administration.

Case 6—N F, female, age 43, married, had been under close observation for 18 months, during which time she had been kept at bed rest in the hospital for 60 days. In June, 1937, she was first told that she had a high blood pressure. Her complaints were weakness, nervousness, nausea, headaches, edema of the ankles and blurring of vision.

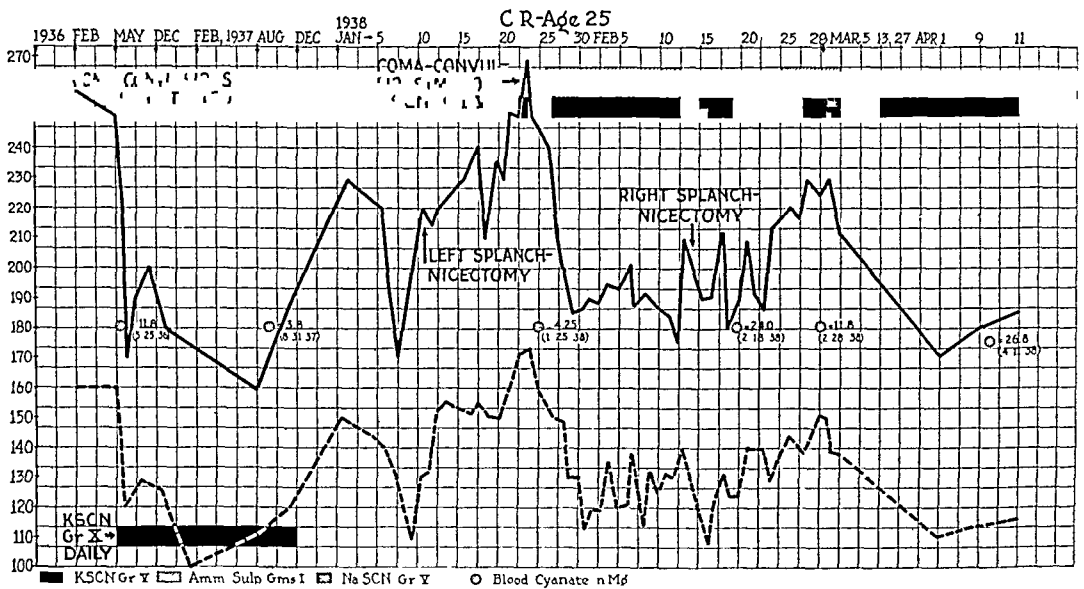


CHART 3—Graph which shows the effect of potassium sulphocyanate given intravenously in patient C R who was in coma and was having convulsions in 1936. All the cyanates were withdrawn and a left splanchnicectomy was done. The patient's blood pressure rose rapidly, the patient became comatose and developed convulsions so that potassium sulphocyanate was again given intravenously. A right splanchnicectomy was done later but the cyanates were continued. This patient requires large doses of cyanates to keep his blood pressure low but shows none of the toxic symptoms which developed from high concentrations of the drug in the blood before operation.

Ophthalmoscopic examination revealed arterial spasm with irregularity in the size of the vessels and blurring of the disk margins. The heart borders were not enlarged and there was no evidence of cardiac decompensation. While under observation in the hospital previously, her blood pressure levels had ranged from 260/163 to 140/88 Mm and at entrance, June 27, 1938, the blood pressure was 192/108 Mm.

On January 5, 1938, the hematocrit reading was 45 per cent, urea nitrogen 11.4 mg, uric acid 4.05 mg, cholesterol 288 mg, chlorides 495 mg, carbon dioxide capacity 54.1 per cent, urine urea 236 mg, urea clearance 30.1 per cent, total proteins 7.35 Gm, albumin 4.21 Gm, globulin 3.09 Gm.

The average resting blood pressure was 193/107 Mm, the cold pressor test was followed by a rise of 38 points in the systolic pressure and six points in the diastolic pressure. Sodium pentothal was given with the control pressure at 210/115 Mm, and during the sleep so induced the mean pressure was 172/109 Mm, the lowest pressure recorded being 156/106 Mm.

On July 1, 1938, a bilateral supradiaphragmatic splanchnicectomy was performed and following this the blood pressure fell precipitately but then gradually rose to 170/96 Mm on the second postoperative day. On July 5, the blood pressure was found to be 230/130

Mm, though, in general, the mean blood pressure readings were consistently lower. Post-operatively, the cold pressor test showed a sharp rise from 190/100 to 230/110 Mm and a prompt fall to 180/96 Mm. The sodium pentothal test following operation produced a fall of the systolic pressure from 180 to 160 Mm three hours after the administration of the drug and then a gradual return after eight hours to 170 Mm. The diastolic pressure on the other hand fell from 106 to 90 Mm after three hours and continued to fall gradually to 76 Mm eight hours after the test, after which it gradually rose again.

On July 18, 1938, when her blood was free from cyanates, the hematocrit reading was 41 per cent, urea nitrogen had risen to 28.3 mg, uric acid was 5.25 mg, cholesterol 248 mg, chlorides 521 mg, carbon dioxide capacity 50 per cent, urine urea 395 mg, urea clearance 22.9 per cent, total proteins 7.03 Gm, albumin 4.20 Gm and globulin 2.83 Gm.

The patient's headaches had disappeared entirely, as had her nervousness, nausea and feeling of fatigue. In general, her subjective symptoms were greatly improved, a fact which has been noted and commented upon generally by all workers irrespective of the type of operation performed.

It was found necessary, however, to begin the administration of potassium sulphocyanate, because the blood pressure levels had risen and the patient's symptoms began to return as she became active about her house. The response to the drug, however, was prompt and effective. Eight months following operation, the patient's general condition has greatly improved and she is carrying on her daily household duties without any complaints. Her blood pressure levels are in the neighborhood of 170/100 Mm on small doses of potassium sulphocyanate, which keep her blood cyanate levels at an average of 12 mg without any evidence of toxic symptoms.

The blood chemistry determination January 6, 1939, showed hematocrit reading 42 per cent, total proteins 6.65 Gm, cholesterol 263 mg, chlorides 538 mg, carbon dioxide capacity 47.7 per cent, urea clearance 39.7 per cent, blood urea nitrogen 22.9 mg, phenolsulphonphthalein 10 per cent in 15 minutes. The cold pressor test showed a rise from 162/106 to 184/114 Mm. The nitroglycerin test showed a fall from 128/72 to 114/72 Mm. The sodium pentothal showed a drop from 140/94 to 120/84 Mm.

Whereas, prior to operation there was hypertrophy of the left heart as compared with the right, six months postoperatively, the size of the heart was within the upper limits of normal and the left side was still slightly larger than the right.

This patient then had not shown a drop in the total proteins of the blood upon sulphocyanate administration before the splanchnic nerves had been sectioned, a response which, after experience, we have learned to expect when the patient responds successfully to the drug. On the other hand, following operation, upon sulphocyanate therapy, there has been a definite response (Chart 4). Moreover, this patient alone showed a more profound reaction to the administration of sodium pentothal following operation characterized particularly by the drop in the diastolic pressure. As we have pointed out before, we believe that the drop in the diastolic pressure is the important factor to be considered in evaluating any effect produced by drugs or operation upon the blood pressure levels.

Experimental Experiences—From the beginning of our interest in this problem, we have carried on experiments in the surgical laboratory in an attempt to duplicate the results on animals and to attempt, if possible, to devise experimental methods which might help us determine how potassium sulphocyanate produces its effect and how section of the splanchnic nerves influences that action.

We chose Goldblatt's method of producing an ischemia of the kidneys by

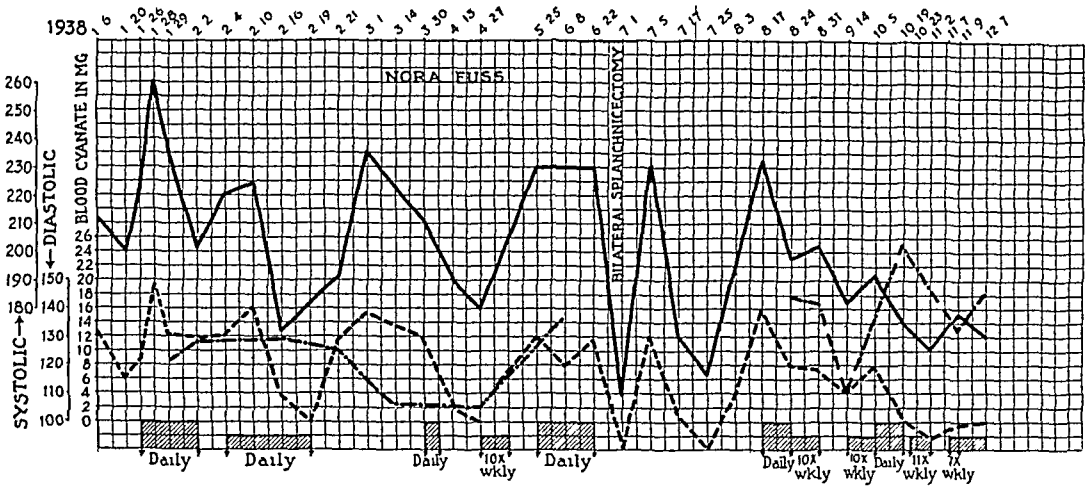


CHART 4—Graph showing blood pressure readings and blood cyanate levels in patient N F before and after bilateral splanchnicectomy While the patient was not as resistant to the cyanates before operation as other patients, following operation her blood pressure can be kept at a low level on small doses of cyanates without any danger of toxic symptoms

placing a clamp on the renal arteries, as the most satisfactory method of producing a hypertension in dogs, which in our opinion simulated hypertension in man as closely as was experimentally possible

Lindberg, Wald and Barker⁵ showed that upon administration of sulphocyanates to normal dogs there was a prompt fall in the blood cholesterol value

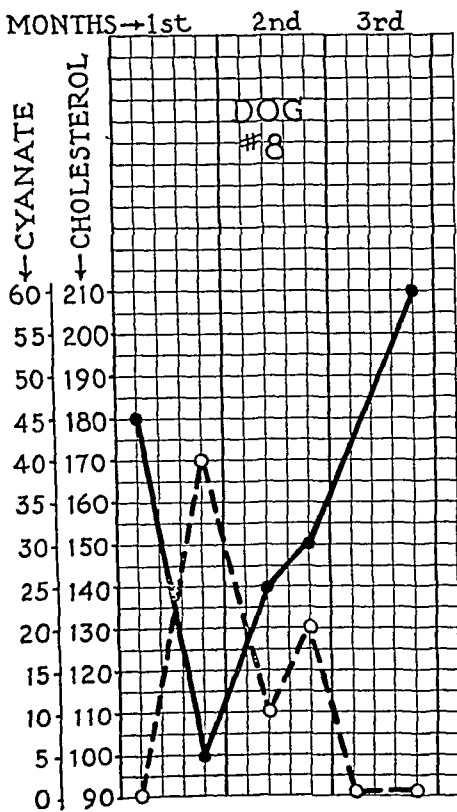


CHART 5—Graph which shows the action of the cyanates (broken line) upon the cholesterol (solid line) in the blood in a normal dog

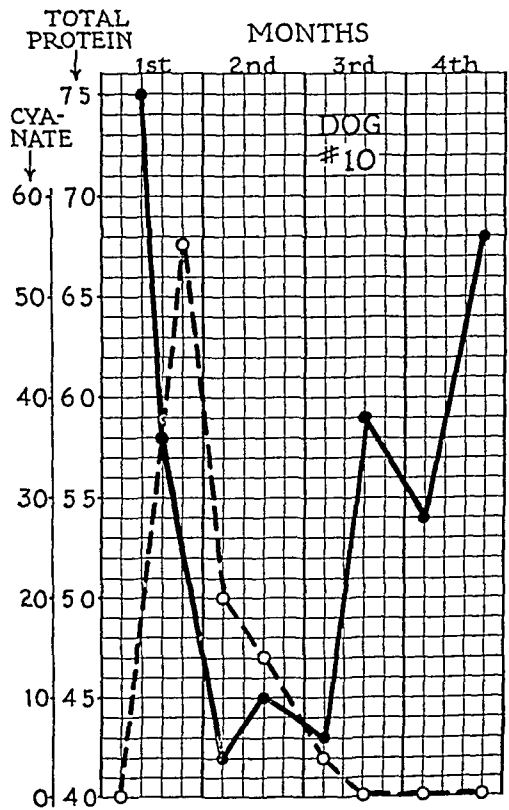


CHART 6—Graph which shows the effect of the cyanates (broken line) on the total proteins of a hypertensive dog (solid line)

and that there is a definite parallel between the elevation of the blood thiocyanate level and depression of the blood cholesterol (Chart 5). Clinically, the response of the blood proteins resembles, in most respects, that of the blood cholesterol (Chart 6). In the presence of this depression of blood protein, either the albumin or the globulin fraction may be more profoundly affected, or both may be equally reduced. Clinically, a depression of the globulin portion with therapeutic doses of the drug has been observed but experimentally, with toxic doses of the drug in dogs there is a proportionate suppression of both the albumin and globulin portions. The fall in the erythrocyte count and the hematocrit in the blood of the dogs was striking. The gradient is in most cases very gradual particularly during the period of administration. Following cessation of administration of the drug, there is a slowing of the fall in the red cell count or an actual cessation of the fall. The hematocrit, which shows a much wider response, tends to stabilize more quickly after the blood is cleared of potassium sulphocyanate.

The livers of dogs fed excessive doses of inorganic sulphocyanate salts show intracellular fatty vacuolization to a marked degree. These changes involve the parenchymal cells, which show practically no tendency toward regeneration or compensatory hyperplasia. Jaundice does not accompany this hepatic degeneration, and although there have been too few opportunities to study the effect of the cyanates upon human tissues, the changes in the blood cholesterol and total protein suggest definite functional hepatic changes.

Bone marrow sections from rib, sternum and femur show a relatively acellular structure. In the least severely intoxicated animals, the normal matrix was replaced by fat but as toxicity became more severe the fatty marrow was replaced by a clear, light, eosin-staining gelatinous material.

Anatomic changes in the adrenal glands were not found in these experiments and chemical analyses of the blood with special reference to sugar metabolism, sodium, potassium and chloride failed to indicate any depression of the function of the adrenal gland.

We have been able to show in every experimental hypertensive dog that administration of potassium sulphocyanate is followed immediately by a drop in the mean arterial pressure. In the hypertensive dog, the hematocrit reading rises, as do the total proteins, blood urea nitrogen and cholesterol in the blood. Following the drop in blood pressure after administration of sulphocyanate there is a parallel drop in the hematocrit, total proteins, cholesterol and blood urea nitrogen. This is well illustrated in the case of "Point," a male, German police dog, and has been confirmed in 10 other animals (Chart 7).

In a group of six dogs, in which the blood pressure level was decreased by the administration of sulphocyanate, bilateral section of the splanchnic nerves supradiaphragmatically was performed after the animals' blood had been freed from the drug. In general, we have observed falls in the blood pressure levels following the operation which have been comparatively more marked and longer maintained than in man, but in every instance there has been a return

able at present and it should come from the combined experiences of more than one group of workers

We can say that our successful results have occurred in the patients who have shown definite responses to tests designed to evaluate objectively the lability of the patient's vasomotor responses. The accumulation of these facts upon a large group of patients from many sources will help answer this question of the value of these tests for operability with finality.

We have been able to duplicate the usual blood chemistry findings present in man with hypertension in dogs in which an experimental hypertension has been produced by renal ischemia. We have been able to reduce the mean arterial blood pressure, the total serum proteins, cholesterol in the blood and the hematocrit reading by the administration of the cyanates. We have not observed a permanent change in the blood pressure level or the blood chemistry findings of these hypertensive dogs after bilateral section of the splanchnic nerves supradiaphragmatically, but the effect of this operation in these animals has been more striking and is maintained longer than in the patients we have studied. We have only suggestive data thus far that in the experimental animals, there is an increased sensitivity to potassium sulphocyanate following splanchnicectomy.

Finally, the mechanism of the action of sulphocyanate still remains to be explained. Westphal and Blum⁶ have suggested that the increase in the blood cholesterol in hypertension causes decreased permeability of the arteriolar muscle cells. They have suggested that sulphocyanate increases this permeability, that the arteriolar portion of the vascular bed relaxes and the arterial blood pressure is thus reduced. It is just as possible that sulphocyanate acts directly upon a pressor substance to modify its effects, or that the drug acts upon glands of internal secretion or their hormones through which the pressor substance acts. Or, it is possible that the hypotensive effect of the cyanates is purely incidental to their more general toxic effects. Vascular relaxation may be simply a part of the depressing effect upon the liver, bone marrow, central nervous system or glands of internal secretion.

Neither our clinical nor our experimental experiences with the problem of hypertension allow us to make any definite statements as yet as to the exact mode or site of action of potassium sulphocyanate in patients with hypertension.

REFERENCES

- ¹ Barker, M. E. The Blood Cyanates in the Treatment of Hypertension. *J. A. M. A.*, **106**, 762, 1936.
- ² Massie, Edward, Ethridge, C. B., and O'Hare, J. P. Thiocyanate Therapy in Vascular Hypertension. *New England Jour. Med.*, **291**, 736, 1938.
- ³ Baer, Samuel, and Slipakoff, Bernard G. Measurements of Circulation Time and the Agents Used in Their Determination. *Am. Heart Jour.*, **16**, 29-43, 1938.
- ⁴ Davis, Loyal, and Barker, M. Herbert. The Surgical Problem of Hypertension. *ANNALS OF SURGERY*, **107**, 899-908, 1938.
- ⁵ Wald, Maurice H., Lindberg, H. A., and Barker, M. H. The Toxic Manifestations of the Thiocyanates. *J. A. M. A.*, **112**, 1120, 1939.
- ⁶ Westphal, K., and Blum, R. *Deutsch. Arch. f. klin. Chir.*, **152**, 331, 1926.

DISCUSSION—DR MAX M PEET (Ann Arbor, Mich) I was particularly impressed in Doctor Davis' communication with the fact that hypertensive dogs—hypertensive because of the Goldblatt clamp—did respond to potassium sulphocyanate The idea of the splanchnicectomy, at least as we do it, is to increase the blood supply to the kidney We believe that in hypertensive patients there is a theoretical Goldblatt clamp—in other words, a continuous vasomotor spasm of the renal vessels The idea of the operation is to remove this neurogenic clamp

The fact that Doctor Davis' dogs with the clamp in place do respond to potassium sulphocyanate shows that the action of the potassium sulphocyanate is not due to an increase in the blood supply to the kidney It must be from some other action

In our medical clinic, sulphocyanates have been employed to a more limited extent perhaps than anywhere else, because our men have not been at all enthusiastic with the results obtained So the series that we have operated upon has not been cases proved definitely to be resistant to sulphocyanate

I am very glad Doctor Davis has limited his cases for operation to that particular group, because through such special studies we may finally obtain a definite knowledge of the whole subject

Tables I, II and III show the results we have obtained in supradiaphragmatic splanchnicectomy in patients who are not sulphocyanate resistant

Table I shows all patients whose preoperative blood pressures averaged over 200 systolic and over 100 diastolic Immediate postoperative blood pressure records have little significance Therefore, all the readings included in this study were made at least six months after operation The longest postoperative period is five years A great many of them belonged in the so-called malignant stage, that is, they had hemorrhages in the eyes, exudates, and a great many of them showed edema either of the retina or of the optic disks The age group, as you will see, is certainly very important There is only one, a girl, age 16, in the 10 to 20 group, but in the 20 to 30 group, there were 17 patients, 13, or 76 per cent, showed definite improvement in blood pressure Even in the age group of 50 to 60, 40 per cent showed a material reduction in blood pressure We established the following standard A reduction in blood pressure, averaged from many readings, must be over 40 Mm systolic and 15 Mm diastolic to be considered significant

TABLE I

AGE DISTRIBUTION OF 90 PATIENTS WITH SIGNIFICANT
REDUCTION IN BLOOD PRESSURE OF A TOTAL OF 194
CASES FOLLOW-UP FROM SIX MONTHS TO FIVE YEARS

Age	Total Cases	Improved	Per Cent
10-20	1	1	100
20-30	17	13	76.5
30-40	54	24	44.5
40-50	92	42	45.7
50-60	30	12	40

The question has been raised, "How permanent is this result?" None of the statistics in Table II were obtained from individuals who had been operated upon less than six months prior to the check-up examination At the time we made this study there were 69 who had only been six to seven months Thirty-nine per cent of these were helped But in a group 9 to 15 months

postoperative, 46 per cent showed improvement and for the 18 to 30 months group, or 42 per cent. That the improvement persists is shown in the group who had gone 33 to 60 months, where 52 per cent still showed a maintained reduction. Our total group of patients, of all ages, shows a maintained worthwhile drop in blood pressure in 46 per cent.

TABLE II

BLOOD PRESSURE REDUCTION IN CASES GROUPED BY
LENGTH OF POSTOPERATIVE PERIOD

Group by Months	Number of Cases	Number Reduced	Percentage Improved
6 mos	69	27	39.2%
9-15 mos	107	50	46.7%
18-30 mos	98	42	42.8%
33-60 mos	48	25	52.0%

We figured not only blood pressure improvement, but also improvement in all the other factors which seem to be influenced either by the high blood pressure or are associated with it. Forty-four per cent have shown a maintained improvement in their water concentration, and the same in urea clearance. Symptomatic improvement was noted by Doctor Davis in a good many of his patients with sulphocyanate. We had 87 per cent of our patients practically free of their symptoms of headaches, dizziness, etc. I think the most significant change, certainly from the economic standpoint, is improvement in incapacitation. Eighty-four per cent have shown worthwhile improvement, and 58 per cent have had complete recovery. This 58 per cent represents a group who were completely incapacitated prior to operation and now are back at their original jobs working as hard as ever (Table III).

TABLE III

PERCENTAGE OF CASES SHOWING IMPROVEMENT FROM
SIX MONTHS TO FIVE YEARS AFTER OPERATION

Blood pressure	46%
Water concentration	44%
Urea clearance	44%
Symptomatic	87%
Incapacitation	84%
(Complete recovery of incapacitation)	58%

Now, perhaps, we can add to this group of 58 per cent another group restored to a useful life by sulphocyanate therapy after splachnicectomy. We have only employed potassium sulphocyanate in three individuals at the University Hospital, after splachnicectomy. I think it is advisable to wait for some time before administering sulphocyanate, because we have had a good many patients whose blood pressure was not improved in the first month or so, but who later showed a gradual improvement over several months.

We do not figure surgical results until at least a six months' postoperative period has elapsed. I think we should wait until after that length of time. If no improvement is noted after the blood vessels have had a chance to recover, then sulphocyanate should be tried. While we have only tried sulphocyanate therapy in three postoperative cases at our hospital, I have frequently suggested to the physicians who have referred cases which did not respond to splachnicectomy that they follow the sulphocyanate treatment as outlined by

Doctor Barker in the Journal of the American Medical Association for March 7, 1936

Of the three that we have had in our clinic, two did not respond to sulphocyanate therapy following splanchicectomy. The third did. That patient was kept on sulphocyanate for some time, then the sulphocyanate was stopped, the blood pressure immediately rose and the symptoms returned. Sulphocyanate was again administered but without improvement.

DR ALFRED BLALOCK (Nashville, Tenn.) I can throw no light on the explanation for these important findings of Doctors Davis and Barker. From an academic viewpoint, it seems to be of particular importance that patients with hypertension and dogs with hypertension due to renal ischemia frequently respond in the same way to this method of therapy. As the experimental evidence increases, it becomes more certain that there must be a great many patients with unexplained hypertension in which renal ischemia is at least a partial factor.

As you may know, if one produces ischemia of one kidney by the use of the Goldblatt clamp, the blood pressure will rise for two or three weeks, and then it is apt to return to the control level. If after this blood pressure returns to the control level, one takes out the opposite normal nonischemic kidney, usually the blood pressure will rise again, which indicates that the nonischemic kidney may be a factor in determining the response to ischemia. This has suggested to a number of workers that the normal kidney may contain or be able to make an antipressor substance which plays a rôle in maintaining the normal blood pressure. Please bear that in mind for a moment, as I will return to it.

In a series of experiments Doctors Levy, Cressman and I determined the effects of intestinal ischemia on the blood pressure. By producing gradual occlusion in multiple-stage operations, we could completely occlude the celiac axis, the superior mesenteric artery and the inferior mesenteric artery. A temporary rise in blood pressure occurred with these procedures, but the pressure returned almost but not quite to the control level.

If, in an animal with intestinal ischemia, one places a clamp upon the artery to one kidney leaving the other kidney undisturbed, in most instances one will get a sustained rise in blood pressure, which in some experiments has persisted now up to 20 months.

As stated, unilateral renal ischemia alone usually results in only a temporary rise in pressure. We have demonstrated the effect of unilateral renal ischemia in an animal in which complete constriction of the main vessels to the intestinal tract had been produced previously. There was a slight rise in blood pressure associated with intestinal ischemia. We then produced constriction of the artery to one kidney, and during a 15-month period this animal was followed, the mean blood pressure remained at the level of approximately 200 mm Hg. Splanchnicectomy had no effect whatever upon the pressure. I might say that this animal became pregnant several months ago, delivered four normal puppies, eclampsia did not occur.

The only point I am trying to make is that it would seem that these experiments throw doubt on the possibility of obtaining from a normal kidney something which will reduce the blood pressure in hypertension.

DR WILLIAM JASON MIXTER (Boston) It seems to me that this paper of Doctor Davis brings up one very interesting point in regard to this whole subject of hypertension. I think we all have to admit that the subject of hypertension is very much mixed up at the present time, the results are not comparable in different clinics, and why we have these different results in

various clinics, we do not know. If we could get closer together in our criteria for our surgical procedures, we might be more in agreement in our results.

I think that what Doctor Davis has done in splitting off a small group of cases and trying to find out what happens with that one individual group, is a very valuable thing, and the more that we can standardize even our own individual criteria and follow them in small groups of cases, the sooner this problem will be decided.

DR GEORGE CRILE (Cleveland) I have had the opportunity in three instances of operating for essential hypertension with a slightly different objective. Seven years ago, I operated upon two cases in which the disease was in a very early stage, the diagnosis being based principally upon the eyegrounds. Within the last week, I have had the opportunity of examining one of these older cases. The patient went through the Clinic and no one who examined him could find any sign of essential hypertension. I mention this because when an early stage of essential hypertension has been established in such cases, such as have been referred to this morning, the fact that surgery can accomplish something worth while for them puts us in a position where we were long ago when considering operation for cancer of the breast for example, or for appendicitis. It was quite a long time before public opinion among the internists agreed that surgery could do something worth while for the patient with early carcinoma. When that fact was established we had the opportunity for operating early. It would seem, from this meager clinical experience, that patients operated upon in the early stage of hypertension that this early operation will be as effective as an early operation is in cases of cancer or in the treatment of appendicitis.

DR LOYAL DAVIS (Chicago) I simply wish to emphasize that the adequate treatment of essential hypertension by cyanates requires the establishment of an accurate blood cyanate level for the particular individual under treatment. This level varies with each individual. In this way, only, can the patient be safeguarded against the symptoms of toxemia which often result from the injudicious employment of cyanates.

Exactly where the cyanates act and how they act is unknown. This remains a problem for physiologic experimentation, and is one in which we are engaged at present.

The excellent experiments of Doctor Blalock and others are important steps, which eventually may lead to the explanation of the entire problem of hypertension and the effect of any procedure which may be carried out. I can only say about Doctor Peet's cases, that I would feel that the cases of many of the patients operated upon who have responded so well to splachnicectomy alone would correspond to the cases of those patients in our group who have reacted definitely and sensitively to small doses of cyanates.

THE RÔLE OF THE PITUITARY GLAND IN WATER BALANCE*†

PETER HEINBECKER, M D ,

AND

HARVEY L WHITE, M D

ST LOUIS, MO

FROM THE DEPARTMENTS OF SURGERY AND PHYSIOLOGY WASHINGTON UNIVERSITY SCHOOL OF MEDICINE AND
BARNES HOSPITAL ST LOUIS, MO

THE PROBLEM of determining the rôle played by the pituitary gland in water balance is not a new one to members of the American Surgical Association. Cushing¹ and his associates were the first to investigate the subject from both the experimental and the clinical standpoints. In their report of 1909, they held the view that the loss of the glandular division of the hypophysis was responsible for the development of diabetes insipidus. This idea was soon abandoned, and, in 1913, they² postulated that a loss of the posterior lobe was responsible. They found it more difficult to correlate this interpretation with the erroneous, but widely accepted, conclusions of Schafer and Herring³ (1905), that the extract of the posterior lobe of the pituitary normally exercised a diuretic function. Von der Velden⁴ (1913) and Faure⁵ (1913) soon reported, however, their successful treatment of diabetes insipidus with pituitin. Numerous clinical and pathologic reports followed, which, on analysis, indicated that the significant organic changes associated with diabetes insipidus were always intracranial, especially those in the region of the hypophysis and hypothalamus. Aschner⁶ (1912) reported that in dogs the loss of the pituitary gland did not result in diabetes insipidus. From this and an analysis of clinical cases, von Hann⁷ (1918) postulated that diabetes insipidus was due to a loss of the posterior lobe but that some anterior lobe must remain present.

Investigators in the field became divided into two groups—the hypothalamists, who held that the hypothalamus was primarily involved in diabetes insipidus, and the hypophysists, who held that the loss of the pituitary gland itself was responsible. Among the former were Camus and Roussy⁸ (1913 to 1925), Bailey and Bremer⁹ (1921), Curtis¹⁰ (1924), Reichert and Danby¹¹ (1936), and Mahoney and Sheehan¹² (1936). Keller and his associates¹³ (1936 and subsequent papers) were first hypothalamists, but in his latest report Keller¹⁴ (1938) states that diabetes insipidus is due to a lack of antidiuretic secreting tissue normally found in the posterior lobe, stalk, and hypothalamus. He finds that a submaximal permanent diabetes insipidus may exist without

* This work was made possible by a grant from the Committee on Scientific Research of the American Medical Association to Dr. Peter Heinbecker, and a grant from the Commonwealth Fund to Dr. Harvey L. White.

† Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

anterior lobe tissue, but that anterior lobe tissue is essential for a maximum diabetes insipidus. Richter¹⁵ (1927 to 1936), Fisher, Ingram, and Ranson¹⁶ (1935 to 1939), and White and Heinbecker¹⁷ (1937 to 1939) regard the essential lesion to be in the neural division of the hypophysis in which term is included the median eminence, infundibular stem, and the pars nervosa. This division of the hypophysis is under the nervous control of the hypothalamico-hypophyseal system. Degeneration of this system leads to degeneration of the pituicytes of the neural hypophysis with a loss of their secreting power.

Neural Hypophysis and the Hypothalamico-Hypophyseal System—In 1915 and in subsequent papers, Tilney¹⁸ showed definitely that in mammals the neural hypophysis is composed of three divisions—the median eminence, the infundibular stem, and the pars nervosa—while the glandular division consists of the pars tuberalis, pars intermedia, and the pars anterior. Cajal¹⁹ (1894), working on the rat, was the first to demonstrate a neural connection between the hypothalamus and the neural hypophysis. Kary²⁰ (1924) revived interest in the subject by redescribing the hypothalamico-hypophyseal tracts and by showing that the supra-optic nucleus may be degenerated in diabetes insipidus. Trendelenburg and Sato²¹ (1928) advanced evidence that an antidiuretic substance could be extracted from tissue of the hypothalamus (median eminence, probably) in the absence of the hypophysis. Maiman²² (1930) demonstrated experimentally degeneration of the supra-optic nucleus following destruction of the tract. Bioeis²³ (1932) reported the occurrence of diabetes insipidus in dogs after bilateral destruction of the supra-optic nuclei or a lesion of the stalk producing atrophy of the former. Beginning in 1935, Fisher, Ingram, and Ranson¹⁶ have published a series of papers in which they showed that permanent polyuria followed the production of lesions limited to the hypothalamus provided that the lesion interrupted the hypothalamico-hypophyseal tracts. Additional evidence pointing to the anatomic and functional similarity of the median eminence, the infundibular stem, and the pars nervosa has been provided by Wislocki and King²⁴ (1936), who showed that on the injection of vital dyes phagocytosis occurred in these three regions and in no other parts of the hypothalamus. The failure of investigators to take cognizance of the facts above described has been responsible for much of the confusion in determining the anatomic basis for diabetes insipidus.

Anatomic Basis for Diabetes Insipidus—To determine the anatomic basis for diabetes insipidus, we have carried out various operative procedures on the hypophysis, the hypothalamus or on both of these structures of more than 100 dogs. The approach was either by the temporal or the buccal route. The lesions consisted of hypothalamic punctures so placed as to interrupt the hypothalamico-hypophyseal tracts (Fig 1A), high stalk sections (Fig 1B) with or without removal of the glandular hypophysis, low stalk sections (Fig 1C) with or without removal of the glandular hypophysis, total destruction and removal of the neural hypophysis (Fig 1D) with removal of the glandular hypophysis. In some animals the glandular hypophysis was removed two to four months after successful hypothalamic puncture. The animals were kept

PITUITARY GLAND IN WATER BALANCE

in metabolism cages for two to ten months on a constant diet of Purina dog chow and meat, milk was sometimes given for a few days postoperatively. Daily urine collections were made, the fluid intake and urine specific gravity were also followed at times. After completion of the period of observation the animals were sacrificed and the brains fixed *in situ*. The hypothalamus together with the skull in the region of the sella turcica was examined microscopically in serially cut 20 micron sections. In this way the extent of the lesion, the condition of the hypothalamic nuclei and of the hypophysis were accurately determined.

In this presentation no attempt will be made to analyze the data secured. The results will be indicated by a brief statement of the findings in some typical experiments.

Following hypothalamic puncture resulting in successful interruption of the hypothalamico-hypophyseal tracts (lesion A, Fig 1), there results a temporary high polyuria (8 to 15 times normal) which in three to eight days is followed by a return to normal or near normal water exchange. This in turn is followed in a few days by a permanent high polyuria (8 to 15 times normal). Microscopically, there is found a disappearance of the cells of the supra-optic and filiform nuclei. There are atrophy and hypercellularity of the neural division of the hypophysis, a large portion of the glandular division is left in a normal state.

When a hypothalamic puncture (lesion A, Fig 1) is made and the glandular division of the hypophysis together with the infundibular stem and pars nervosa are removed at the same operation, there follows an immediate polyuria (five to ten times normal) lasting three to eight days which is followed by a period of normal or near normal fluid exchange lasting eight to 20 days. Then there follows a rather sudden increase to a permanently elevated fluid exchange four to eight times the normal. When the median eminence is also removed in this type of operative procedure (lesion D, Fig 1) the normal interphase is or tends to be eliminated. Microscopically, the cells of the supra-optic and filiform nuclei are found absent, the median eminence is atrophied or absent (if removed at operation) and there is no trace of pars nervosa or glandular hypophysis.

If, in animals in which a successful interruption of the hypothalamic tract (lesion A, Fig 1) has resulted in a permanent high polyuria, a nearly complete removal of the glandular division of the hypophysis is carried out two to four months after the original puncture, there results no diminution in poly-

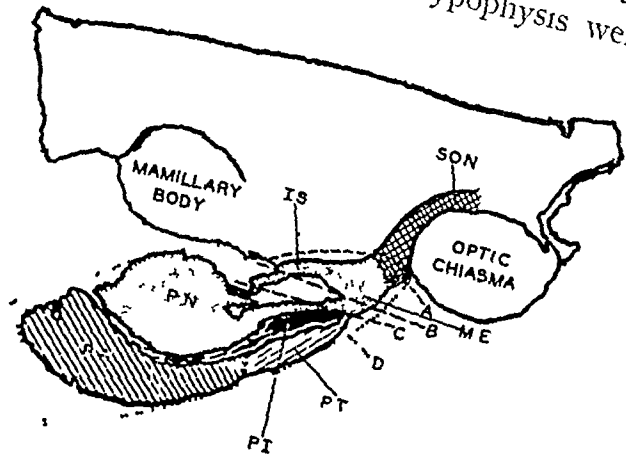


FIG 1—Drawing of sagittal section of dog's hypothalamico and hypophyseal regions indicating the extent of operations designated A, B, C and D in the text. SON, supra-optic nuclei, ME, median eminence, IS, infundibular stem, PT, pars tuberalis, PN, pars nervosa, PA, pars anterior.

uria Microscopic sections of the hypothalamus and skull of nine such animals have shown that we have not succeeded in removing entirely all of the anterior lobe. In each instance, 3 to 5 per cent of the pars anterior has been found embedded in the scar tissue at the posterior end of the sella. In seven instances, it was felt that the microscopic appearance of the cells remaining warranted the belief that they were capable of functioning. It was not possible to exclude the possibility in the two instances where the cells did not have a normal appearance. The amount of anterior lobe present was not enough to prevent atrophy of the gonads and a narrowing of the adrenal cortex.

In animals in which a high stalk section (lesion B, Fig 1) was made there developed a moderate temporary polyuria one to three times the normal of one to three days' duration, followed by a return to permanently normal water exchange level. Microscopically, such brains showed an estimated loss of about 50 per cent of the cells of the supra-optic and filiform nuclei. The pars nervosa was atrophied and hypercellular, the glandular division of the hypophysis and the median eminence were essentially unchanged.

Animals in which a low stalk section (lesion C, Fig 1) was made with or without removal of the pars nervosa and glandular division of the hypophysis, showed no increase in fluid exchange or a very temporary one of one to three days' duration. Microscopically, the brain showed a 30 to 50 per cent atrophy of the supra-optic and filiform nuclei, a normal median eminence, an absence of the remainder of the hypophysis in those instances where its removal was attempted. When not removed the pars nervosa became atrophied, the anterior lobe remained normal. It seems clear that the anterior lobe receives an adequate blood supply from below or through newly established channels after its complete separation from the brain and even that small fragments of the stalk left behind in the sella in an attempted complete removal may survive.

Analysis of the above results permits the statement that a maximal polyuria never follows unless there is a complete loss of the supra-optic and filiform nuclei.

The Rôle of the Anterior Lobe in Water Balance—Our experimental results indicate that the permanent phase of diabetes insipidus resulting from removal of the neural division of the hypophysis is less than the maximal possible when the glandular division of the hypophysis is also removed at the same operation. When the glandular division is removed two to four months after maximal diabetes insipidus (8 to 15 times normal) has been established by hypothalamic puncture its loss *seems* to have no consequences. It is not possible to state definitely that the small residual fragment of anterior lobe (3 to 5 per cent) found in all our dogs of this class is of no consequence, but our present evidence speaks in favor of this view. Experimental proof is being obtained to settle the point. It is felt that under normal conditions the anterior lobe plays a diuretic rôle. Elsewhere in this paper, it will be shown that it acts synergistically with the secretion of the thyroid gland in stimulat-

ing water excretion. It is possible to remove or destroy part of the neurohypophysis in such a way that the presence or absence of polyuria depends upon the presence or absence of anterior lobe. These findings indicate a diuretic effect of the anterior lobe, they are not incompatible with our present belief that the anterior lobe is not essential to the maintenance of a maximal and permanent polyuria previously established by a *complete destruction of all elements of the neurohypophysis*. While, as stated above, the evidence for this belief is not at present complete, we can state positively that maintenance of a maximal and complete polyuria is not impaired by removal of 95 to 97 per cent of the anterior lobe.

The Effect of Thyroid on Urine Output—When 0.1 Gm. of desiccated thyroid per kilo is fed to normal dogs the increase in urine output usually ranges from zero to 50 per cent. Thyroidectomy in normal dogs produces slight if any permanent decrease in urine output. When thyroidectomized dogs are given the above dose of desiccated thyroid their urine output is little if any increased.

It has been held by Baines, Regan, and Bueno²⁵ (1933) and others that the action of pituitary anterior lobe extract is mainly through stimulating the thyroid gland. To test this hypothesis experiments were carried out on dogs, some of which had been modified by various operative procedures, with the following results.

It was found that the daily administration of 1.7 to 2 cc. of anterior lobe extract (0.25 gr. fresh tissue per cc.) per kilo of body weight usually increases the urine output of normal dogs two- to fivefold, the increase appears within the 24 hours and lasts three to six days. Similar results were obtained in the hypophysectomized dogs recovered from the transient polyuria.

The daily administration for six to eight days of 0.1 gr. of desiccated thyroid per kilo produces no significant change in the daily urine output of either hypophysectomized or hypothysectomized-thyroidectomized dogs. The daily addition for two days of 2 cc. of anterior lobe acid extract per kilogram during a period of thyroid administration, beginning after six to eight days of thyroid, produces in hypophysectomized dogs an increase in daily urine output about the same as the anterior lobe alone. Daily administration for two days of 2 cc. of anterior lobe extract per kilo does not produce any increase in urine output in the hypophysectomized-thyroidectomized dog within the first few weeks after thyroidectomy but may produce an increase, although smaller than in the normal or thyroid-fed animal, if given two months or later after thyroidectomy. The daily administration for two days of 2 cc. of anterior lobe extract per kilo to the hypophysectomized-thyroidectomized dog during a period of thyroid administration (0.1 gr. per kilo daily) shows results essentially the same as those seen in hypophysectomized dogs before thyroidectomy (Chart 1).

Effect of Thyroidectomy in Experimental Diabetes Insipidus—The effect of thyroidectomy on the transient phase of diabetes insipidus is to abolish it within 24 to 48 hours. Such an effect is, however, not obtained when thy-

oidectomy is carried out during the permanent phase of polyuria. In the latter case the effect apparently depends upon the length of time which has elapsed after destruction of the neural division of the hypophysis. The earlier in the permanent phase thyroidectomy is carried out, the greater is its antidiuretic effect. After four to six months it was found in the two dogs so investigated that no effect at all on urine output resulted from thyroidectomy. It can be stated on the basis of our observations and those of Ranson and his collaborators²⁶ (1938) that usually no more than a 50 per cent decrease in polyuria, and often less, can be expected from thyroidectomy when a state of diabetes insipidus exists in dogs and cats.

Effect of Thyroidectomy in Human Diabetes Insipidus—A similar finding to that observed in experimental diabetes insipidus resulted in one human case. A male, colored, age 55, with central nervous system syphilis and diabetes insipidus of three years' duration, which had not yielded to antidiuretic therapy, was completely thyroidectomized in August, 1936. The pre- and postoperative findings are shown in Chart 2. After thyroidectomy, there was a 25 to 30 per cent decrease in urine output on a normal diet with unrestricted salt intake. The patient insisted that his thirst and polyuria were much less disturbing than before operation. On a low-salt diet the average 24-hour urine output after thyroidectomy was essentially the same as on the same diet before thyroidectomy. The urine volume was increased less by salt ad-

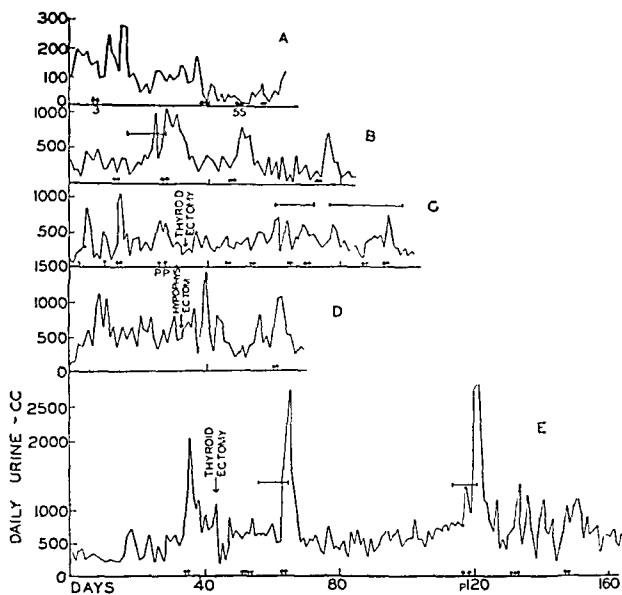


CHART 1.—desiccated thyroid 0.1 gm per kilo
A = anterior lobe extract 1.7 to 2 cc per ilo P = Phylene
Where more than two cubic centimeters per kilo of extract
were given, the figure under the arrow designates the dose
in cubic centimeters per kilo. A = normal female monkey,
B = male dog, hypophysectomized 15 days before beginning
of chart, C = male dog, hypophysectomized three months
before beginning of chart, D = male dog, hypophysectomized as indicated on
chart, E = male dog, hypophysectomized 18 days before
beginning of chart, thyroidectomized as indicated on chart

ministration and diminished more by pitressin after operation than before.

The findings indicate there exists in beef anterior lobe extracts a diuretic principle which cannot act in the absence of thyroid in the acutely thyroidectomized animal but does have a moderate effect in the chronically thyroidectomized animal. That this diuretic principle is not merely the thyrotropic hormone is indicated by the finding that with a constant intake of thyroid by mouth, insufficient in itself to produce diuresis, the thyroidectomized dog shows a diuretic response to anterior lobe administration which is not effective without the thyroid. The effect of the thyroid appears to be that of a sensitizing agent for the diuretic principle of the anterior lobe.

PITUITARY GLAND IN WATER BALANCE

Experiments to determine whether the ability of the thyroid to render effective the diuretic action of anterior lobe is specific or is due to its effect on general metabolism have been reported by White, Henbecker, and Robertson²⁷ (1938) (Chart 3). Dogs were rendered moderately diabetes insipidus by incomplete hypothalamic puncture, this polyuria was reduced but not abolished by subsequent thyroidectomy. When 0.1 g of desiccated thyroid is now given to such animals the polyuria is restored essentially to the pre-

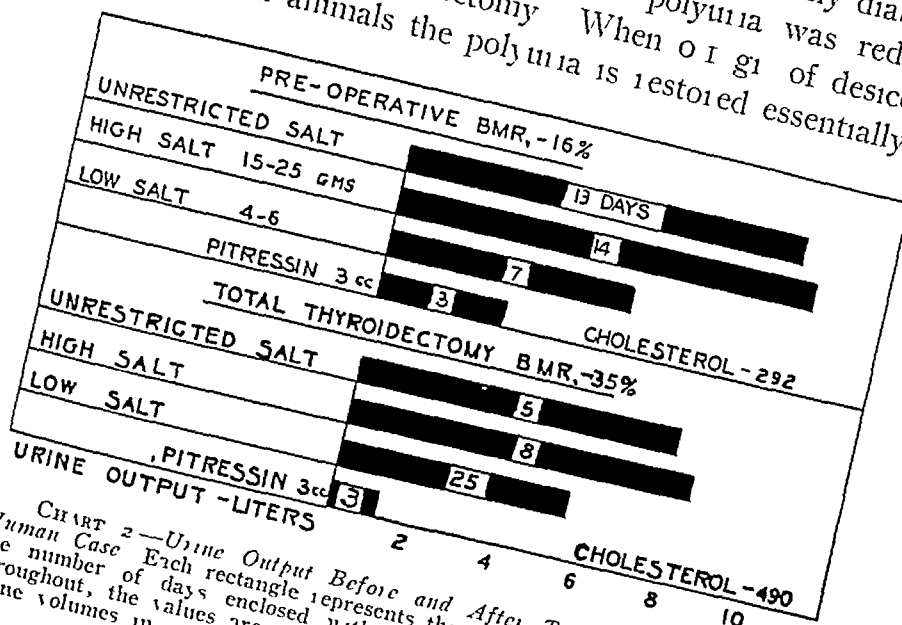


CHART 2—Urine Output Before and After Total Thyroidectomy in Human Case. Each rectangle represents the average 24 hour urine flow for the number of days enclosed within it. Fluid intake was unrestricted throughout, the values are not recorded because they closely paralleled the urine volumes in every period.

thyroidectomy level. However, a daily dosage of 3 mg of dinitrocresol per kilo (which produced the same elevation of basal metabolic rate as the above thyroid dosage) has no diuretic effect. This indicates that the action of thyroid, which is synergistic with the diuretic action of anterior lobe, is probably not due to the former's effect in elevating the basal metabolic rate.

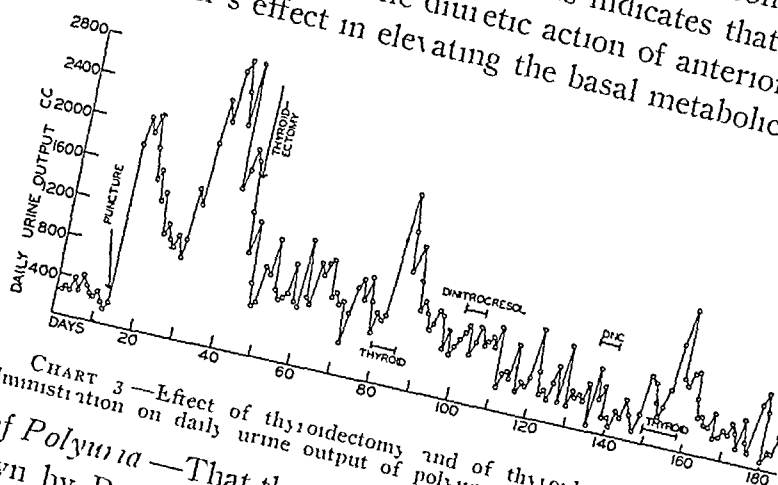


CHART 3—Effect of thyroidectomy and of thyroid and dinitrocresol administration on daily urine output of polyuric dog.

Primacy of Polyuria—That the polyuria and not the polydipsia is primary, has been shown by Richter¹⁷ (1927), Fisher, Ingram and Ranson²⁶ (1938) and by others. We have confirmed the observations of these investigators in this matter.

Site of Action of Pitressin—It has been held by some, that the site of action of pitressin is in the kidney and by others in the body tissues generally or in some hypothetic water center of the hypothalamus. It is considered by us

that pitressin acts on the kidney for the following reasons. First, Starling and Verney²⁸ (1926) have shown that pitressin administered in doses which do not affect blood pressure acts as an antidiuretic on the isolated perfused kidney. Second, it has been shown repeatedly that pitressin does not alter the water or salt content of the blood plasma in normal or diabetes insipidus animals or the colloidal osmotic pressure in normal animals. Third, if pitressin is given to an individual after a large drink of water, diuresis is prevented even when the amount of blood dilution is such as would cause a diuresis had no pitressin been administered.

Transient and Permanent Phases of Diabetes Insipidus and Normal Interphase—Following any of the above operative procedures, there may appear

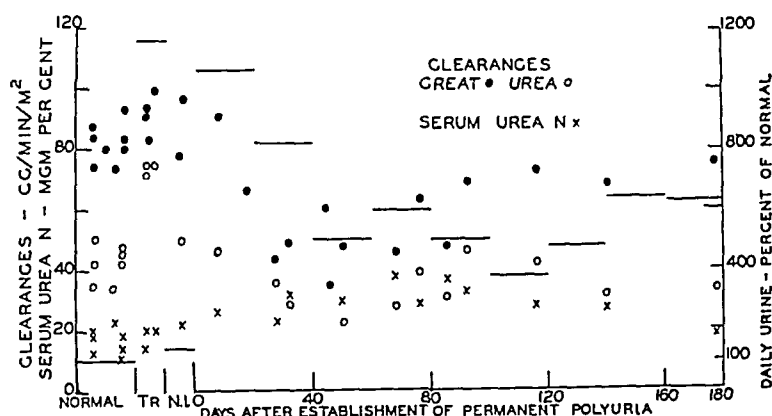


CHART 4—Daily urine output in averages of 20 day periods, creatinine and urea clearances and serum urea N before and after establishment of polyuria. This chart shows the findings on five diabetes insipidus dogs. Urine outputs are expressed as percentages of the normal, averaged for 20 day periods in all five dogs and shown as the horizontal lines. Left section of figure, labeled Normal, shows urine output (100 per cent) and clearances during the preoperative observation periods of 24 to 53 days with the various dogs. Transitory phase of polyuria Tr and normal interphase NI. Horizontal axis expresses time quantitatively after zero day.

a transient increase in fluid exchange varying from two to ten times the normal. It makes its appearance from several hours to 24 hours after operation. It lasts from one to 10 or 12 days and is then followed by a return to a normal or nearly normal level of fluid exchange (normal interphase). In those instances where there has been a severance of the neural division of the hypophysis from its neural connections with the supra-optic and filiform nuclei of the hypothalamus, this normal interphase is followed in five to 20 days by a rather sudden return to an increased fluid exchange essentially as great as occurred during the transient phase. This is called the permanent phase of diabetes insipidus. The transient phase is considered to be due to a functional elimination of the pituicytes by injury. On recovery a normal fluid exchange results because then secretion is reestablished. When a normal interphase precedes a permanent polyuria, its duration is considered to coincide with the time necessary for denervated pituicytes to lose their secretory functions.

Creatinine and Urea Clearances in Diabetes Insipidus and Hypophysectomized Dogs—*Diabetes Insipidus*. In general, creatinine clearance is unchanged during the transitory polyuria. Urea clearance is somewhat elevated

but this is probably because of the greater urine flow. Creatinine and urea clearances during the normal interphase between the transitory and permanent polyurias are normal. These clearances remain normal for one to two weeks after the onset of the permanent polyuria and then both gradually fall, creatinine reaching a level approximately half the normal by four to six weeks after operation. Urea clearances fall less than creatinine and may not fall at all even with 50 per cent fall in creatinine, this may result in an unusually high rate of urea to creatinine clearance values. This situation is complicated by the fact that, on the average, the urine flows during the clearance periods of the permanent polyuria were somewhat higher than during normalcy or latent period. This would work in the direction of raising urea clearances. A slight fall or no change under our conditions might have been a more definite fall if urine flow rates could have been kept constant during all clearance periods. The values have returned not quite but almost to normal after 175 days of permanent polyuria. The above statements are based on 20 creatinine and 22 urea clearance values made on five dogs preoperatively and at various times after production of a lesion which resulted in permanent diabetes insipidus, where each clearance value is the average of three consecutive 30-minute clearance periods (Chart 4).

Hypophysectomy—Creatinine and urea clearances fall after hypophysectomy with polyuria and are returning toward normal at the end of a few weeks (Chart 4).

Response of Dogs with Diabetes Insipidus to Water Administration—The response of five dogs with diabetes insipidus to the administration of 3 per cent of body weight of water given by stomach tube has been compared with that of 13 normal dogs and three hypophysectomized dogs without polyuria. Urine samples were obtained every 15 minutes by catheterization for four or more periods, the water was then administered by stomach tube and urine samples again collected every 15 minutes for three to four hours or until the urine flow reached a normal level. Blood salt dilution was determined by measuring the serum specific conductivity in terms of ohmic resistance at in-

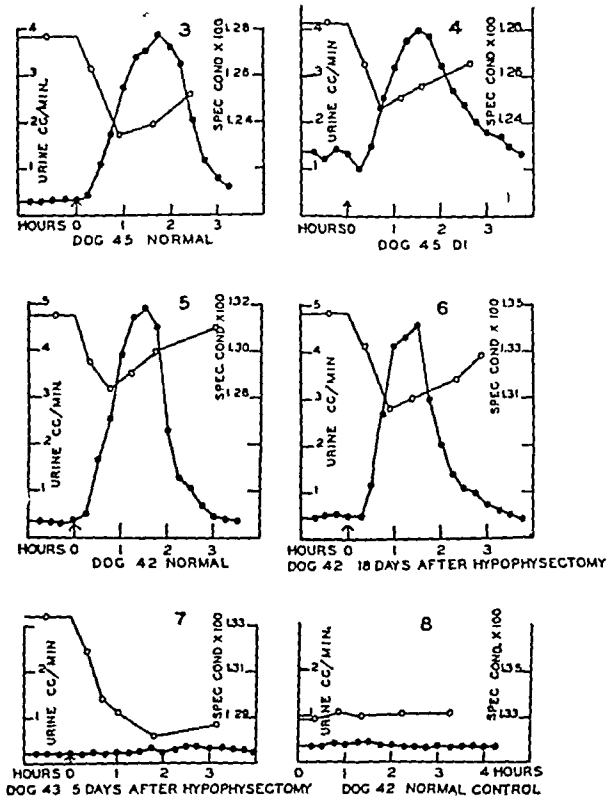


CHART 5—Serum electrolyte dilution and urine output responses of dogs to 3 per cent body weight of water, serum specific conductivity in reciprocal ohms, urine output in cubic centimeters per minute. Three per cent body weight of water by stomach tube at zero hour except in Figure 8, which shows a control, i.e., normal dog with no water administration.

tervals before and after the water administration, in some cases serum viscosity was also followed as an index of protein content. Typical response curves are shown in Chart 5.

The results indicate that the diuretic responses of normal dogs, hypophysectomized dogs without polyuria and diabetes insipidus dogs are similar. It is of interest to note here that, in contrast, the chronic human diabetes insipidus patient shows little or no diuretic response to 3 per cent body weight of water by mouth. For reasons not yet understood, dogs during the first 10 days after hypophysectomy also show little or no diuretic response to such a dose of water. The results do not support the view of Verney and his collaborators²⁹ (1933) that the lag in water output behind water load represents the time for preformed pitressin to disappear. In our diabetes insipidus dogs there was presumably little or no preformed pitressin present and still the lag was similar to that found for the normal dog.

TABLE I

AVERAGE CONCENTRATION OF URINE AFTER 24 HOURS OF WATER DEPRIVATION

	Specific Gravity	Creatinine Mg Per Cent	Urea N Mg Per Cent	NaCl Mg Per Cent
Normal preoperative	1.068	190	4270	1100
Postoperative diabetes insipidus	1.035	145	1670	860
Normal preoperative	1.064	220	4100	1050
Postoperative hypophysectomized	1.040	160	2100	1020

Effect of Water Deprivation in Dogs with Diabetes Insipidus—The effect of depriving diabetes insipidus and hypophysectomized dogs without polyuria of water for 24 hours is shown in Table I. The figures represent the averages obtained on three dogs of each type before and after operation. Diabetes insipidus dogs can concentrate to a specific gravity of about 1.030, but normal dogs can concentrate up to a specific gravity of 1.065. Neither the normal nor the hypophysectomized dogs show any greater concentration after 48 hours than after 24 hours. The diabetes insipidus animal can hardly tolerate more than 24 hours of water deprivation. After that time, gradually developing weakness becomes marked and unconsciousness supervenes. Restorative measures, in the form of intravenous normal saline, are effective if given early after the development of such symptoms.

SUMMARY AND CONCLUSIONS

Experimental evidence is presented to indicate that diabetes insipidus results only after functional or anatomic removal of all the neural hypophysis, *i.e.*, pars nervosa, stalk, and median eminence.

The anterior lobe, while not essential for the existence of the permanent state of diabetes insipidus, normally probably plays a diuretic rôle.

The diuretic effect of the anterior lobe is not exerted solely through its

thyrotropic action not in the maintenance of a normal basal metabolic rate. The anterior lobe and the thyroid appear to be synergistic.

Total thyroidectomy in human diabetes insipidus may result in a diminution of urine output of approximately 30 per cent. On the basis of experimental evidence, it would be expected to vary from zero to 50 per cent.

Creatinine clearance is unchanged during the transitory phase of experimental diabetes insipidus. Urea clearance is somewhat elevated, probably because of increased urine flow. During the normal interphase period both clearances are normal. Creatinine clearance reaches a level approximately half the normal by two to four weeks after the onset of permanent polyuria. It remains down for a variable time and then gradually returns toward normal, which may be almost reached after six months of permanent polyuria. Urea clearance falls less than does creatinine clearance during the phase of permanent polyuria and may not fall at all. Serum urea rises as clearances fall early in permanent polyuria but shows a later return toward normal.

Hypophysectomized or diabetes insipidus dogs, in which exists a more or less complete chronic deficit of pituitrin, show no significant alteration from the normal in the time relations of their blood dilution and urine output responses to ingestion of 3 per cent body weight of water. This is interpreted as indicating that the lag of maximum rate of water output behind maximum blood dilution after water drinking in the normal is not due to the time required for preformed pituitrin to disappear. Within the first week or 10 days after hypophysectomy there may be only a slight and delayed diuretic response to water by mouth.

After 24 hours of water deprivation, the ability of hypophysectomized dogs without polyuria and of diabetes insipidus dogs to concentrate urine is impaired about 50 per cent with respect to urea, 25 per cent with respect to creatinine, and unchanged with respect to chlorides. The ability of hypophysectomized dogs without polyuria to tolerate water deprivation is as great as that of the normal but that of diabetes insipidus dogs is greatly decreased.

The authors wish to acknowledge permission to reproduce Charts 2 and 3 from Volumes 36 and 38 of the *Journal of the Society of Experimental Biology in Medicine*, and Charts 1, 4 and 5 from Volumes 118 and 123 of the *American Journal of Physiology*.

BIBLIOGRAPHY

- ¹ Cushing, H. *Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System*. C. C. Thomas, Springfield, Ill., 1932.
- ² Cushing, H. *Boston Med and Surg Jour*, **168**, 901, 1913.
- ³ Schafer, E. A., and Herring, P. T. *Proc Roy Soc London*, **77**, 591, 1905.
- ⁴ Von der Velden, R. *Berl klin Wchnschr*, **1**, 2083, 1913.
- ⁵ Farini, A. *Gaz d Osp*, **34**, 1135, 1913.
- ⁶ Aschner, B. *Arch f d ges Physiol*, **146**, 1, 1912.
- ⁷ Von Hann, F. *Frankf Ztschr f Path*, **21**, 337, 1918.
- ⁸ Camus, J., and Roussy, G. *Compt rend Soc de biol*, **75**, 483, 628, 1913.
- ⁹ Bailey, P., and Bremer, F. *Arch Int Med*, **28**, 773, 1921.
- ¹⁰ Curtis, G. M. *Arch Int Med*, **34**, 801, 1924.
- ¹¹ Reichert, F. L., and Dandy, W. E. *Bull Johns Hopkins Hosp*, **58**, 418, 1936.

- ¹² Mahoney, W, and Sheehan, D Brain, 59, 61, 1936
- ¹³ Keller, A D, Noble, W, and Hare, W K Am Jour Physiol, 117, 467, 1936
- ¹⁴ Keller, A D Arch Surg, 37, 760-771, November, 1938
- ¹⁵ Richter, C P Quart Rev Biol, 2, 307-343, 1927
- ¹⁶ Fisher, C, Ingram, W R, and Ranson, S W Arch Neurol and Psychiat, 34, 124, 1935
- ¹⁷ White, H L, and Heinbecker, P Am Jour Physiol, 118, 276, 1937
- ¹⁸ Tilney, F Jour Comp Neurol, 25, 213, 1915
- ¹⁹ Cajal, S Ramon y Anales de la Sociedad Española Historia Natural, 24, 214, 1894
- ²⁰ Kary, C Virchows Arch f path Anat, 252, 734, 1924
- ²¹ Trendelenburg, P, and Sato, G Verhandl Deutsch Pharmakol Gesellsch, 114, 114, 1928
- ²² Maiman, R M Neurol u Psychiat, 129, 666, 1930
- ²³ Broers, H Experimenteele diabetes insipidus Diss Inaug Kemmk en Zoon, Utrecht, 1932
- ²⁴ Wislocki, G B, and King, L S Am Jour Anat, 58, 421, 1936
- ²⁵ Barnes, B O, Regan, J F, and Bueno, J G Am Jour Physiol, 105, 559, 1933
- ²⁶ Fisher, C, Ingram, W R, and Ranson, S W Diabetes Insipidus and the Neuro-Hormonal Control of Water Balance A Contribution to the Structure and Function of the Hypothalamico-Hypophyseal System Edwards Brothers, Inc, Ann Arbor, Mich, 1938
- ²⁷ White, H L, Heinbecker, P, and Robertson, E P Proc Soc Exper Biol and Med, 38, 439, 1938
- ²⁸ Starling, E H, and Verney, E B Proc Roy Soc B, 97, 321, 1925
- ²⁹ Verney, E B, and associates Proc Roy Soc B, 112, 521, 1933

DISCUSSION—DR LOYAL DAVIS (Chicago) The hypothalamus and the hypophysis are very closely associated anatomically and functionally. In the past, it has been very difficult, experimentally, to produce a lesion of the hypophysis without producing injury to a hypothalamus. Consequently, in the literature there has grown up a group of "hypothalamists" and a group of "hypophysists," each of whom believes that the results of their experimental work have been due to a lesion of the hypothalamus or, on the other hand, to removal of the hypophysis.

Diabetes insipidus constituted a very perplexing problem, to which many investigators have paid attention. Clinically this has been of great interest to neurologic surgeons because of the association of diabetes insipidus with tumors apparently confined to the hypophysis.

Recent refinements in operative technic and experimental surgery have made it possible to remove a portion of the hypophysis or all of that gland without damage to the hypothalamus, as Doctor Heinbecker has shown in his work which has been controlled by serial sections of the midbrain. From another standpoint, Doctor Heinbecker's results may be caused as due to a lesion of the hypophysis alone because they are duplicated by results obtained by Doctor Ranson as the result of producing an electrolytic lesion with the Horsley-Clarke stereotactic instrument.

It seems to me that the whole problem which Doctor Heinbecker presents so well, resolves itself to a statement that diuretic processes are entirely under control of the anterior lobe of the hypophysis. This is quite distinct from the old view that these processes were under the control of the posterior lobe. Therefore, polyuria may be thought of as resulting from an uncompensated activity of the anterior lobe or a disease and, therefore, the result of an imbalance between the anterior and posterior lobes of the hypophysis. There is

still some difference of opinion as to the exact manner in which the anterior lobe exercises this diuretic influence

Doctor Ranson and his associates, working upon thyroidectomized cats, have obtained results similar to those of Doctor Heinbecker. Their work is, however, contrary to that of Mahoney and Sheehan who found that diabetes insipidus, produced in dogs by a lesion of the stalk of the pituitary gland, could be made to disappear after a thyroidectomy. As both Ranson and Heinbecker point out, there is a strong probability that the polyuria of Mahoney's and Sheehan's dogs was not a permanent one.

Finally, to emphasize the importance of the small area in the midbrain known as the hypothalamus, I need only to remind you that just a few millimeters away from the point where Doctor Heinbecker has performed his operations and where Doctor Ranson has made his lesions, are the periventricular nuclei. At the Toronto meeting of this Association some years ago we showed that a lesion of those nuclei prevented the diabetes mellitus which could be reproduced in animals by the removal of the pancreas though the hypophysis was untouched and remained intact.

THE CONTROL OF WATER AND ELECTROLYTE BALANCE IN SURGICAL PATIENTS^{*}

J RUSSELL ELKINTON, M D , MONROE T GILMOUR, M D

AND

WILLIAM A WOLFF, PH D

PHILADELPHIA, PA

FROM THE SURGICAL SERVICES AND THE AHER CLINICAL LABORATORY OF THE PENNSYLVANIA HOSPITAL PHILADELPHIA PA

THE MANAGEMENT of water and electrolyte balance is one of the most important aspects of modern surgery. Although this subject began to receive attention in the treatment of cholera a century ago,¹ the general problem has been elucidated only within recent years.² As a result of fundamental work in biochemistry and physiology a new point of view has developed in the treatment of intestinal obstruction, severe burns and other conditions showing a disturbance of electrolyte and water balance. Practical methods for the management of these conditions in surgical patients have been proposed by several authors,³⁻⁷ the value of which methods is attested by a literature too voluminous for citation here.

Because of certain limitations in methods proposed to date, further studies were undertaken. The present report describes a routine developed at the Pennsylvania Hospital for the control of electrolyte and water balance in patients undergoing serious surgical procedures. Emphasis is placed on simultaneous determination of hematocrit values, plasma protein and total base as giving a fairly accurate picture of the state of hydration and electrolyte balance.

Physiologic Considerations—From the physiologic standpoint three factors must be considered in the care of patients with a disturbance of the water and electrolyte balance: (1) The degree of hydration, (2) the electrolyte balance and (3) the state of nutrition. These factors will be reviewed briefly.

The water of the body may be divided into three fractions: Intracellular, interstitial, and intravascular. These fractions and the shift of water between them are graphically illustrated by Gamble.⁸ The interstitial and the intravascular fractions together make up the extracellular water. The interstitial fraction is normally about three times as large as the intravascular, and is a great reservoir whose volume fluctuates widely in varying degrees of hydration while that of the intravascular fraction (plasma volume) is maintained at a constant level. This extensive reservoir of interstitial water, or "swamp," as Cannon⁹ calls it, may be relatively "wet" or "dry," but it maintains a steady volume in the vascular tree or "river."

The essential problem in estimating the degree of hydration is the determi-

^{*} Read before the Philadelphia Academy of Surgery, May 1, 1939. Submitted for publication July 27, 1939.

nation of the volume of water in the "swamp" and the "river," the extracellular volume. At the present time, methods for the direct measurement of the extracellular water volume¹⁰ have not been adopted as a routine clinical procedure. Direct weights showing serial changes are suggestive, but these are difficult to obtain in clinics where accurate stretch scales are not available for bedridden patients, and frequently patients are received in a dehydrated state where the normal weight is not known. Practically, aside from clinical signs the extracellular water volume can be approximated only by considering indirect evidence obtained from its intravascular portion, the plasma.

Plasma volume is maintained at the expense of interstitial water during extracellular water loss, up to a certain point.¹¹ Beyond this point, the plasma volume diminishes with resulting hemoconcentration. Hemoconcentration or diminished plasma volume, therefore, indicates a serious depletion of the extracellular reservoir,¹² but does not measure that depletion quantitatively.

One of the simplest clues to plasma volume is the hematocrit which measures the relative proportion of plasma to erythrocytes*. In the absence of progressive changes in the total number of erythrocytes, such as with hemorrhage or with transfusion, serial hematocrit values reflect changes in plasma volume.¹³ Although shifts in pH cause some variation in the volume of the erythrocyte and thereby affect the hematocrit value,¹⁴ such changes are negligible in comparison with those resulting from alterations of plasma volume. Likewise, changes in plasma protein concentration, where there is no protein addition or loss, may reflect changes in plasma volume. These determinations, therefore, may be used to advantage in detecting more serious degrees of dehydration.

The actual amount of water held in the extracellular reservoir is dependent on the amount of total base (mostly sodium) present.^{2b, 15a} The electrolyte concentrations of the intra- and extracellular body fluids are maintained at a remarkably constant level.^{2c} Loss of electrolytes with a parallel loss of water from the extracellular fluid compartment does not produce changes in electrolyte concentrations.¹³ Only when the extracellular reservoir of base and water is seriously depleted is there a fall in total base concentration in the plasma. The total base concentration by itself, however, gives no indication as to the total amount of base and water lost.

Not only the total base concentration but the relative proportion of acidic and basic constituents is important in a patient with an abnormal loss of fluid containing electrolytes. Such loss of fluid may result in acidosis or alkalosis, in addition to dehydration. Determination of plasma carbon dioxide combining power and plasma chlorides, from which the total base concentration may be approximated, is important in following the patient's electrolyte status.

A detailed discussion of the nutritional requirements of the seriously ill surgical patient will not be attempted here. The importance of an adequate

* Erythrocyte counts or hemoglobin concentrations can be used, but in the present study the hematocrit has seemed to be the simplest way to follow this factor.

intake of carbohydrates and vitamins is well known. Protein metabolism in surgical patients has received wide attention recently. Definite levels of plasma protein are necessary to maintain the plasma osmotic pressure¹⁶. The rôle of the edema of hypoproteinemia in the prevention of wound healing has been stressed by Ravdin¹⁷. Because of these considerations, a knowledge of the plasma protein level is important.

The combination of repeated simultaneous hematocrit, plasma protein, carbon dioxide combining power, and chloride determinations gives valuable

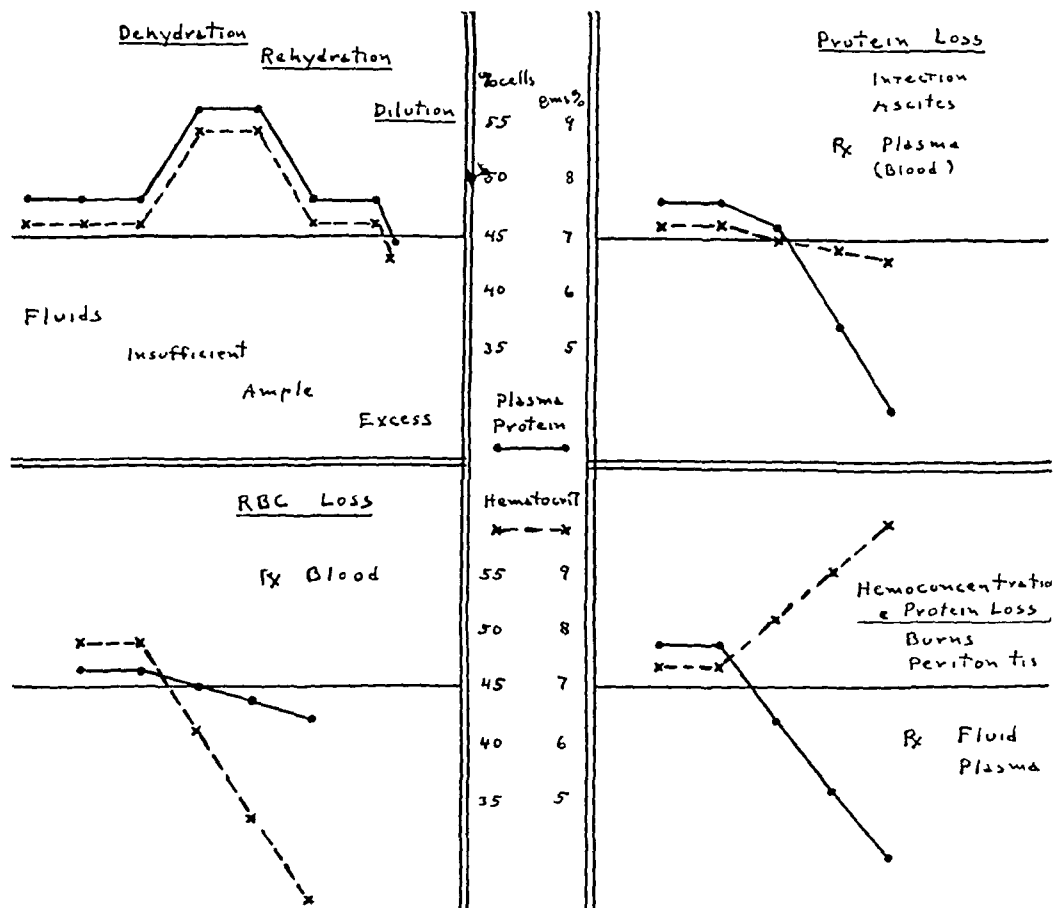


CHART 1—Hypothetic curves showing the main types of changes in plasma protein and hematocrit values observed in this series

information for controlling certain types of patients. The main types of variations of plasma protein and hematocrit values (Chart 1) correspond roughly to those which occur in cases of abnormal gastro-intestinal fluid loss, infection, hemorrhage and burns.

The degree of hydration in such cases may be estimated from these four main values, considered together with clinical signs. This is especially helpful when the patient is first seen in a dehydrated state where previous daily total fluid intake and output are not known. When the patient is under observation the daily total fluid balance, intake and output, is followed, water loss from vaporization being estimated. The volume and specific gravity of urine are

also valuable indices. But in the present study the combination proposed above has seemed to give a more reliable indication of the fluid balance in the patient, as well as indicating the erythrocyte and plasma protein levels.

Methods—The simplicity of making these determinations routinely should be stressed. A single sample of blood, 5-6 cc, drawn without stasis into an absolutely dry syringe, is transferred directly into a Sanford-McGath hematocrit tube containing an adequate amount of heparin. After centrifuging, the hematocrit is read. With a few drops of plasma the protein may be readily calculated from its specific gravity as determined in Barbour and Hamilton's falling-drop apparatus¹⁸. The remaining plasma is then used for a determination of the carbon dioxide combining power and chloride concentration.

Extracellular electrolyte concentrations have commonly been expressed in a number of different units, such as volumes per cent, milligrams per cent, and equivalents of 0.1 N NaCl. As Gamble¹⁹ and Butler²⁰ have so clearly pointed out, a complete picture of the electrolyte pattern is possible only if all of its components are expressed in the same unit, preferably milliequivalents per liter.*

Since a solution containing electrolytes is electrically neutral, the equivalent concentration of positive or basic ions must be exactly equal to the equivalent concentration of negative or acidic ions. Therefore the total base concentration may be calculated by an estimation of the total acid concentration. The latter value may be calculated from the plasma carbon dioxide combining power and plasma chloride concentration^{17b} by converting these figures to milliequivalents per liter and adding 25 M eq/L for the remaining acid radicals, as follows:

$$\begin{aligned}\text{CO}_2 \text{ comb power} &= 60 \text{ vol } \% \times 0.45^* = 27 \text{ M eq/L} \\ \text{Chlorides (as NaCl)} &= 600 \text{ mg } \% \times 0.17^* = 103 \text{ M eq/L} \\ \text{"R" (HPO}_4^-, \text{SO}_4^-, \text{organic acid, protein)} &= 25 \text{ M eq/L}\end{aligned}$$

$$\text{Total acid} = \text{total base} \qquad \qquad \qquad = 155 \text{ M eq/L}$$

* Conversion factors for changing the usual units to milliequivalents per liter

Specimens of urine collected at the same time as the blood sample is taken should be examined for albumin and acetone, and, in the absence of evidence of marked renal damage, ketosis, or hypoproteinemia, "R" may be assumed to equal about 25 M eq/L.¹⁹ The resultant figure for total base, although not absolutely correct, is sufficiently accurate for most clinical purposes.

Therapy—The routine just described gives very definite indications as to the type of fluid needed. A low or falling hematocrit value usually indicates the need for whole blood transfusions. A low protein concentration is a prime

* A milliequivalent is the equivalent weight of an ion or molecule in milligrams. For example, one milliequivalent per liter means 23 mg of sodium ion, 61 mg of bicarbonate ion or 35.5 mg of chloride ion, respectively, per liter of solution.

indication for plasma transfusion when the hematocrit value is normal or above normal (as in burns). Protein is supplied while at the same time blood cells are not added to a vascular system already relatively overloaded with them. Maintenance of the plasma protein level with intravenous amino-acids as reported by Elman and Weiner²¹ has not been attempted in this study.

Parenteral fluids are given to a great majority of patients according to relatively simple rules. Normal saline (usually containing 5 per cent glucose)

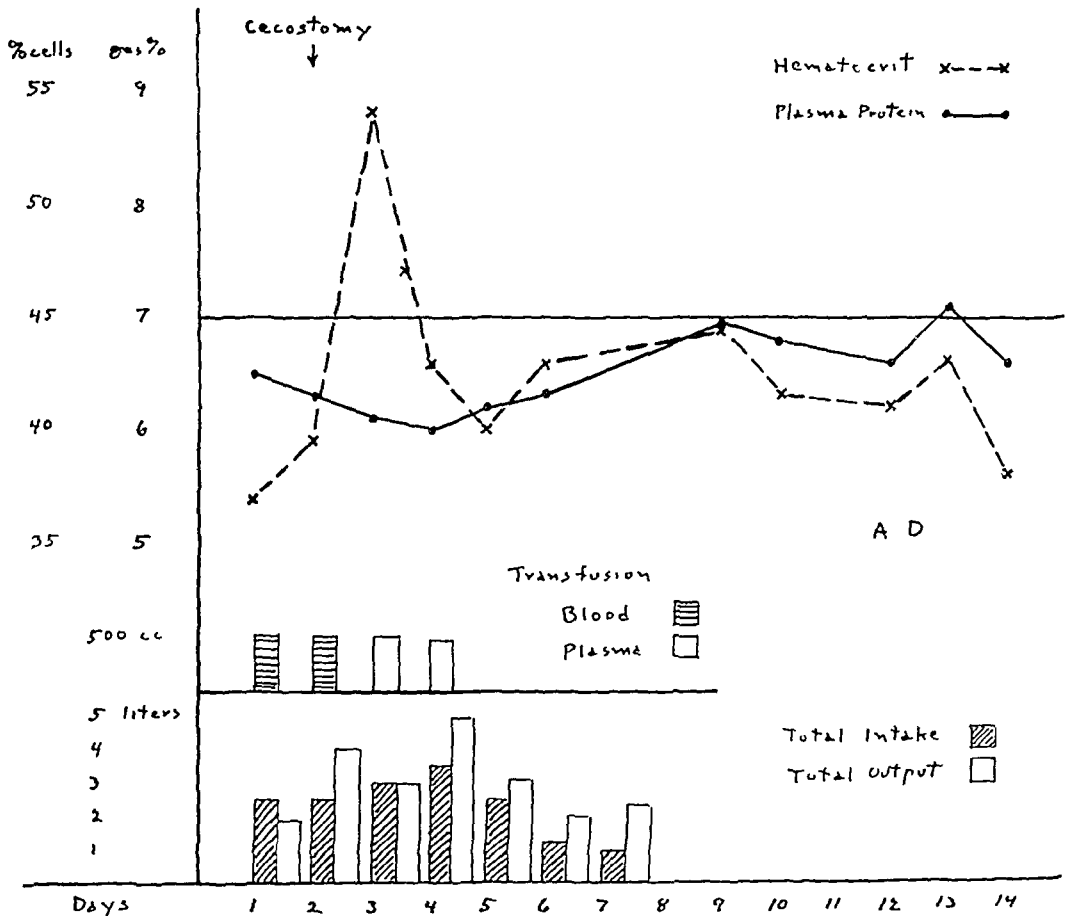


CHART 2 - Case 1. Illustrates the following points:

- (1) Marked rise in hematocrit following a negative fluid balance of one day (the day of operation) which suggests previous depletion.
- (2) Lack of simultaneous rise of proteins suggesting a loss of protein and indicating plasma transfusion.
- (3) Satisfactory postoperative course despite several negative balances.

is given in equal volumes to replace losses of abnormal fluids (gastric, biliary, pancreatic, intestinal) which never exceed physiologic saline concentration, plus an allowance of 1 to 5 Gm of sodium chloride for urinary excretion. The balance of water for insensible loss, estimated to be between one and two liters, is given as a solution of 5 per cent glucose in distilled water. Under this regimen most patients showed an adequate urinary output of one liter per day.

The estimation of electrolyte needs in the patient with a serious water and electrolyte depletion has been attempted in several ways. One easy method

WATER AND ELECTROLYTE BALANCE

is to replace abnormal fluid losses with equal volumes of normal saline,¹ as mentioned above. Another, which in this study has been found to be somewhat unreliable, is to control the salt administration by following the urinary chloride concentration.^{7, 6} In cases with marked acidosis, Haitmann²² has proposed the quantitative use of sodium lactate to raise the carbon dioxide combining power. Collier and coworkers³ have proposed a formula for replacement of sodium chloride based on the plasma chloride levels. These

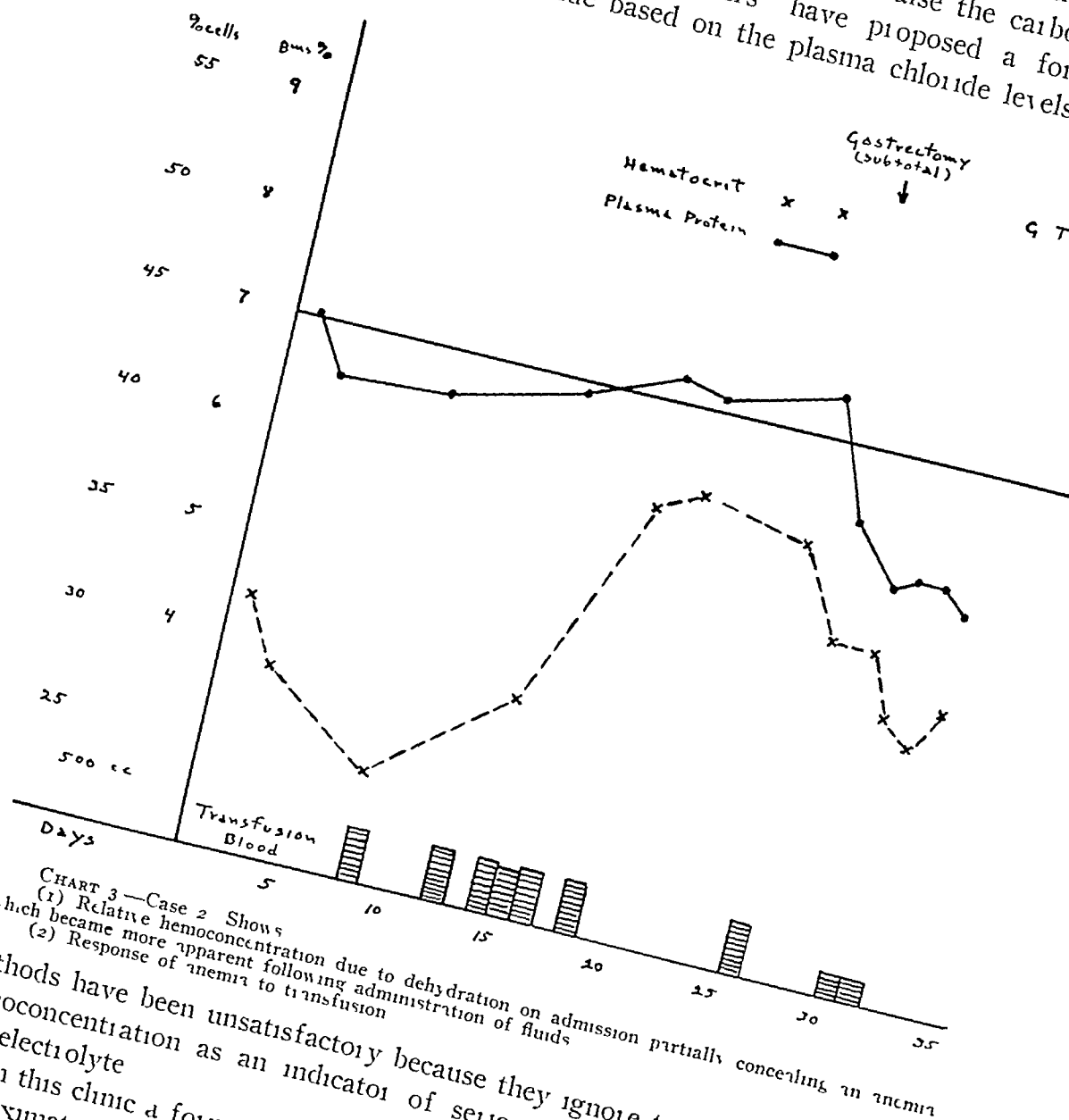


CHART 3—Case 2 Shows
(1) Relative hemoconcentration due to dehydration on admission partially corrected by administration of fluids
(2) Response of anemia to transfusion

methods have been unsatisfactory because they ignore total base as such and hemoconcentration as an indicator of serious losses of extracellular water and electrolyte.

In this clinic a formula has been worked out and used which is only a first approximation of the amount of base required. This formula is based on three assumptions. First, that the relative loss of interstitial fluid in dehydration is at least equal to the relative decrease in the plasma volume, secondly, that the electrolyte pattern of the interstitial fluid is qualitatively the same as in plasma and thirdly that electrolyte needs calculated from plasma concentra-

tions (corrected for normal plasma volume) may be extended to the entire extracellular volume. This calculated amount of base with an adequate amount of water will restore the depleted extracellular fluid volume to a point somewhat beyond that necessary for maintenance of a normal plasma volume but not necessarily to a normal state.

Because 90 per cent of the base in the extracellular fluid is sodium, all calculations and base replacements may be conveniently referred to the sodium

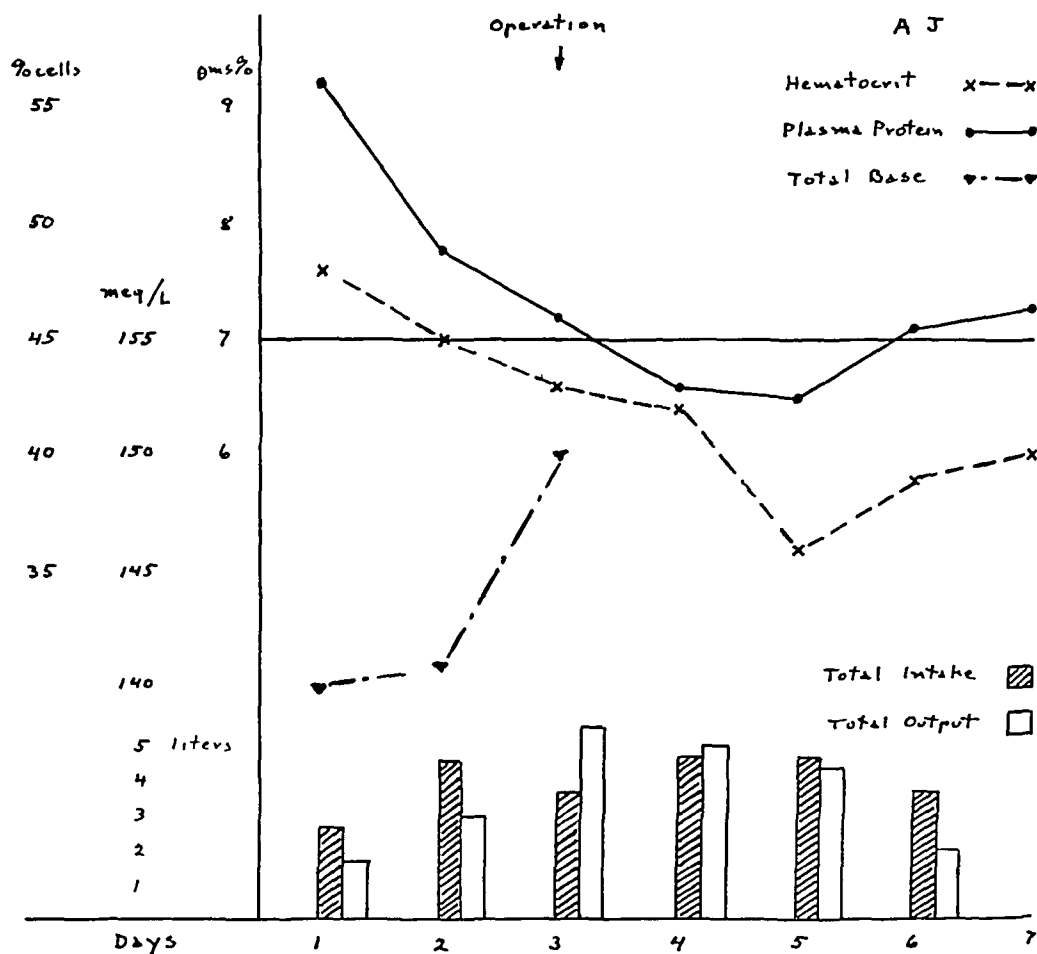


CHART 4—Case 3. Shows the initial dehydration indicated by a high hematocrit and plasma protein, a low total base, and their response to water and electrolyte therapy.

The calculated sodium ion requirement is given as sodium chloride, sodium bicarbonate, or sodium lactate, according to the requirement for acid ions.

The derivation of the formula follows. The observed concentration of plasma total base in milliequivalents per liter (B) is corrected by the ratio of the plasma protein concentration in grams per cent at normal hydration (P_n) to the observed plasma protein concentration (P_o). This value is subtracted from 155, the normal concentration of extracellular total base in milliequivalents per liter. The difference is multiplied by a factor made up of the equivalent weight of sodium, 23, multiplied by 0.2 of the body weight in kilograms (W), which is the approximate fraction of the body made up of extracellular fluid,¹⁰

multiplied by 0.001 to change milligrams to grams. The result is the grams of sodium ion required.

$$\text{Gm Na}^+ \text{ required} = 0.0046 W \left(155 - \frac{P_{nB}}{P_o} \right)$$

The same calculation can be made using hematocrit instead of plasma protein values. However, the ordinary hematocrit reading as observed (H_o) and the reading at normal hydration (H_n) are converted to plasma volume and expressed as a ratio of plasma volumes per unit volume of cells, which is the factor desired for correcting the observed plasma total base concentration (B). This ratio is expressed thus:

$$\frac{(100 - H_o) H_n}{H_o} \div (100 - H_n), \text{ or } \frac{(100 - H_o) H_n}{(100 - H_n) H_o}$$

The final equation therefore becomes:

$$\text{Gm Na}^+ \text{ required} = 0.0046 W \left(155 - \frac{(100 - H_o) H_n B}{(100 - H_n) H_o} \right)$$

The sodium ion requirement can be converted into grams of sodium chloride, sodium bicarbonate, and sodium lactate, by the factors 2.5, 3.6, and 4.9 respectively.

The accuracy of the calculations of the base requirement by either of the above equations depends upon knowing or being able to estimate fairly accurately the hematocrit value or plasma protein concentration at normal hydration. In the anemic patient where the hematocrit value at normal hydration is not known, the plasma protein may offer a more accurate basis for calculation. Where neither the hematocrit nor plasma protein values at normal hydration can be estimated, the formula cannot be used. In such cases more empiric methods are required, such as giving fluids up to 6 per cent of the body weight.

The application of this formula is illustrated in Case 5, L. Del Q., as follows:

Body weight at normal hydration	= 95 Kg
Initial total base	= 132 M eq /L
Initial hematocrit	= 62 per cent cells
Estimated hematocrit at normal hydration	= 40 per cent cells

Calculated sodium ion requirement =

$$0.0046 \times 95 \times \left(155 - \frac{(100 - 62) \times 40 \times 132}{(100 - 40) \times 62} \right) = 44.1 \text{ Gm Na}^+$$

Actual amount of base given (net)	= 35.6 Gm Na ⁺
Final hematocrit	= 41 per cent cells
Final total base	= 152 M eq /L

The results of the application of this formula in a small series of patients are tabulated in Table I. It must be remembered that it is the net sodium ion

requirement being calculated, allowance should be made for simultaneous sodium losses

TABLE I

RESULTS OF THE APPLICATION OF FORMULA FOR CALCULATION OF THE SODIUM ION REQUIREMENT

Patient	Body Weight at Normal Hydration Kg	Initial Total Base M eq /L	Initial Hemato-crit or Protein % Cells Gm %	Hemato-crit or Protein at Normal Hydration % Cells Gm %	Calculated Base Requirement Gm Na ⁺	Actual Amount Base Given Gm Na ⁺	Time Interval Hours	Final Hemato-crit or Protein % Cells Gm %	Final Total Base M eq /L
L Del Q	95	132	62	40	44 1	35 6	48	41	152
A J	85	140	9 2	7 0	19 2	17 6	48	7 2	150
J H									
Period I	62	134	48	40	16 5	21 0	72	45	145
Period II	62	140	55	40	22 6	17 8	84	38	158
Period III	62	138	52	38	24 5	22 2	72	38	151
F G	60	138	37 5	30	15 5	16 3	72	32	164

Although the above formula stresses the need for base, the requirements for acid ions and water must be kept constantly in mind. Electrolyte and water losses in dehydration should be replaced in physiologic proportions. About three-quarters of the total base requirement is usually given as isotonic saline and the remainder as sodium lactate or bicarbonate. In the presence of a lowered carbon dioxide combining power or chloride concentration in the plasma, these constituents must be restored to normal levels by the administration of additional sodium chloride, bicarbonate, or lactate as indicated. Disregard of these precautions in replacing electrolytes may lead to a dangerous alkalosis or acidosis. The sole aim of this procedure is the restoration and maintenance of physiologic concentrations and amounts of basic ions, acid ions, and water.

All efforts to regulate electrolyte and water balance depend ultimately upon the activity of the kidney. This organ must excrete or conserve base in accordance with body needs, dispose of surplus acid ions by forming ammonium salts which appear in the urine, eliminate metabolic waste products, and control the water content of the blood. In performing these functions the kidney in a normal adult produces one or two liters of urine per day. Water deprivation to the point of reduced urine output interferes with renal control of acid-base balance and causes a retention of urea and other products. Correction of acidosis, alkalosis and dehydration with physiologic saline is possible only because the kidney functions properly. Even then, one or two days may be required for the attainment of normal conditions. Definite advantages result from the parenteral administration of electrolytes and water in physiologic proportions and amounts as recommended in this paper. The acid-base

imbalance is corrected within a few hours. The kidney is spared the burden of eliminating the unnecessary electrolytes.

The use of the values—hematocrit, plasma protein, and total base estimated from chloride and bicarbonate—is illustrated in the appended ten cases.

In the charts, a base line is drawn at 7 Gm per cent and 45 per cent cells as a simple convenience. Actually there should be "a normal zone" between 6 and 8 Gm per cent and 40 and 45 per cent cells. As regards intakes and outputs, the total intake includes all oral and parenteral intake. The total output includes urine, vomitus, any drainage from the gastro-intestinal and biliary

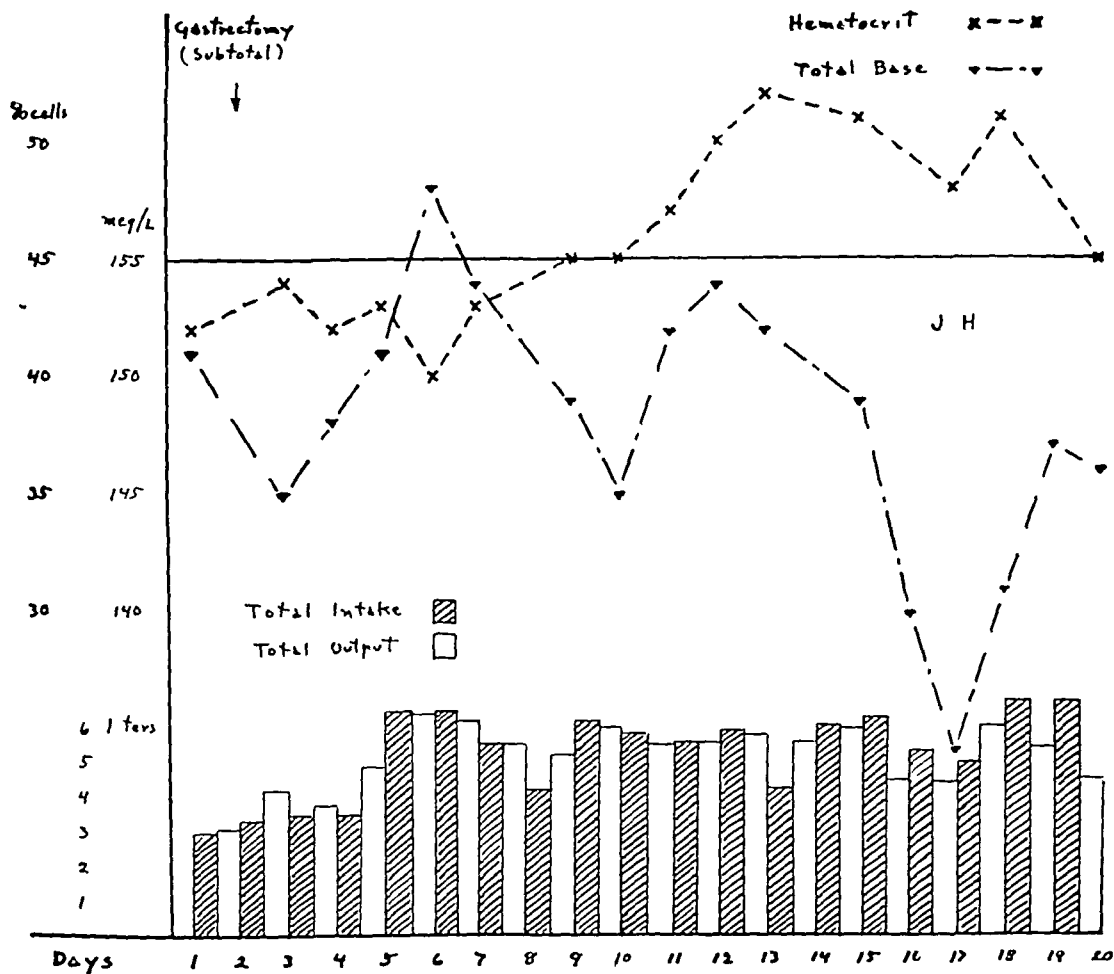


CHART 5—Case 4. Shows the first 20 postoperative days and illustrates the slow building up of a negative fluid balance, a diminished fluid reserve is indicated by a rising hematocrit before the total base falls to significantly low levels.

tracts and water of vaporization which is approximated between one and two liters, depending on the patient's size, temperature, and the weather. The probable error in the total output is at least 200 cc.

ILLUSTRATIVE CASE REPORTS

Case 1—A D, Negress, age 57, had been vomiting and showed signs of intestinal obstruction of one week's duration. A cecostomy was performed for large bowel obstruction due to carcinoma of the descending colon. The carcinoma was later removed by the Mikulicz procedure (Chart 2).

Case 2—G T, white, male, age 49, was diagnosed as having a carcinoma of the stomach. Following a period of building up of the red cell level, a subtotal gastrectomy was performed. Convalescence was satisfactory (Chart 3).

Case 3—A J, Negress, female, age 40, had had vomiting, obstipation and abdominal distention for three days. At operation an adhesive band constricting the terminal ileum was released. Convalescence was uneventful (Chart 4).

Case 4—J H, Negro, male, age 54, had had a subtotal gastrectomy performed for a gastric ulcer, which was followed by complete and partial obstruction caused by post-

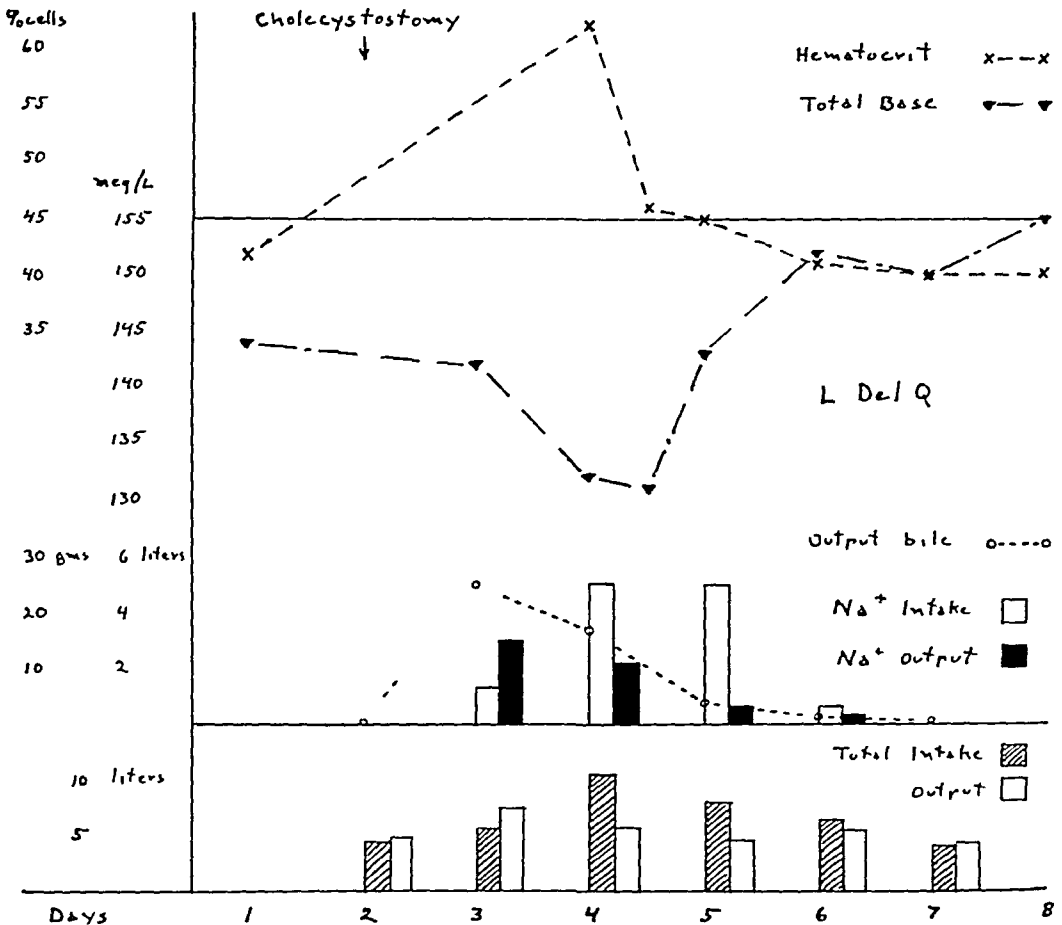


CHART 6—Case 5 Shows

- (1) Rapid and severe dehydration due to a sudden excessive loss of sodium salts and water
- (2) The moderate reduction in total base level is deceptive because it does not indicate the enormous loss of electrolyte, recognizable only by considering hemoconcentration in conjunction with total base level
- (3) The hematocrit first indicating a satisfactory response to therapy while the total base still remained low
- (4) The positive sodium ion balances necessary to restore the patient to completely normal levels

operative adhesions for 40 days, necessitating a second celiotomy and jejunostomy. During this time he was sustained entirely by parenteral therapy. Subsequent recovery.

Case 5—L Del Q, white, female, age 42, suffered from diabetes, severe obstructive jaundice and pain. Cholecystostomy performed and a common duct stone was subsequently passed. Between the twelfth and thirty-sixth postoperative hours 5,000 cc of bile drained externally, and patient became severely dehydrated and anuric. She responded to massive parenteral therapy. Convalescence was uneventful (Chart 6).

* We are indebted to Elizabeth Dudley, B S, M S, Department of Pediatrics, School of Medicine, University of Pennsylvania and the Children's Hospital of Philadelphia, for the sodium determinations on this patient.

WATER AND ELECTROLYTE BALANCE

Case 6—H B, white, male, age 33, had had a liver abscess aspirated at celiotomy, with subsequent peritonitis and death. Autopsy revealed very extensive multiple liver abscesses and fluid in the abdominal cavity (Chart 7)

Case 7—H W, white, male, age 58, had had a posterior gastrojejunostomy performed for obstruction of the duodenum due to carcinomatosis. Postoperatively, the patient bled from his stoma and, despite a reoperation, died (Chart 8)

Case 8—J P, Negro, male, age 43, sustained first and second degree burns of both lower arms and hands. Treated locally with tannic acid and silver nitrate. Subsequent convalescence was uneventful, and no skin grafts were necessary (Chart 9)

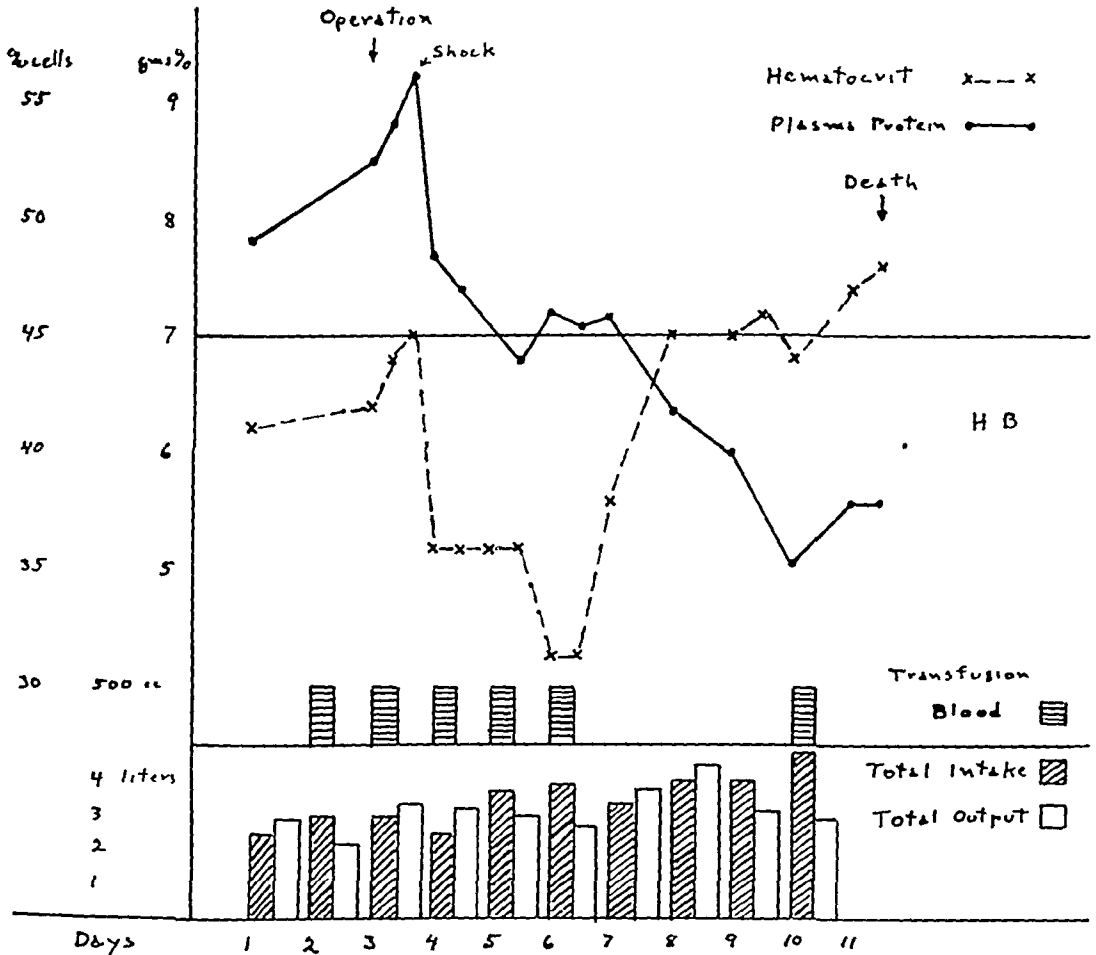


CHART 7—Case 6 Shows
(1) The extremely severe shock immediately after operation and the response to therapy
(2) The secondary dehydration as evidenced by the rising hematocrit
(3) The marked loss of protein when at the same time the hematocrit was rising. Plasma transfusions should have been given during this period

Case 9—J C, white, female, age 14, sustained second and third degree burns of entire back, buttocks, posterior surface thighs, and right hand (20 to 25 per cent of the body surface). Treated locally with tannic acid and silver nitrate. Systemic reaction fifth and sixth days. Recovery without skin grafts (Chart 10)

Case 10—A R, white, male, age 25 months, sustained second and third degree burns over entire back and most of chest and abdomen. Immediate tanning with tannic acid and silver nitrate and subsequent skin grafting. Acutely toxic and moribund on third day, with improvement following the administration of adrenal cortical extract (Chart 11)

Discussion—Strict control of electrolyte and water balance was necessary in less than 10 per cent of the surgical patients in the wards of the Penn-

sylvania Hospital. Studies were begun on admission of every patient showing clinical signs of dehydration, intestinal obstruction, or severe burns, and also on those patients in whom extensive surgery of the gastro-intestinal tract was anticipated. Prolonged biliary or gastric drainage was considered an imperative indication for electrolyte and water balance control. Prompt quantitative replacement of the proper fluids has reduced the expected mortality rate and facilitated recovery in many instances.

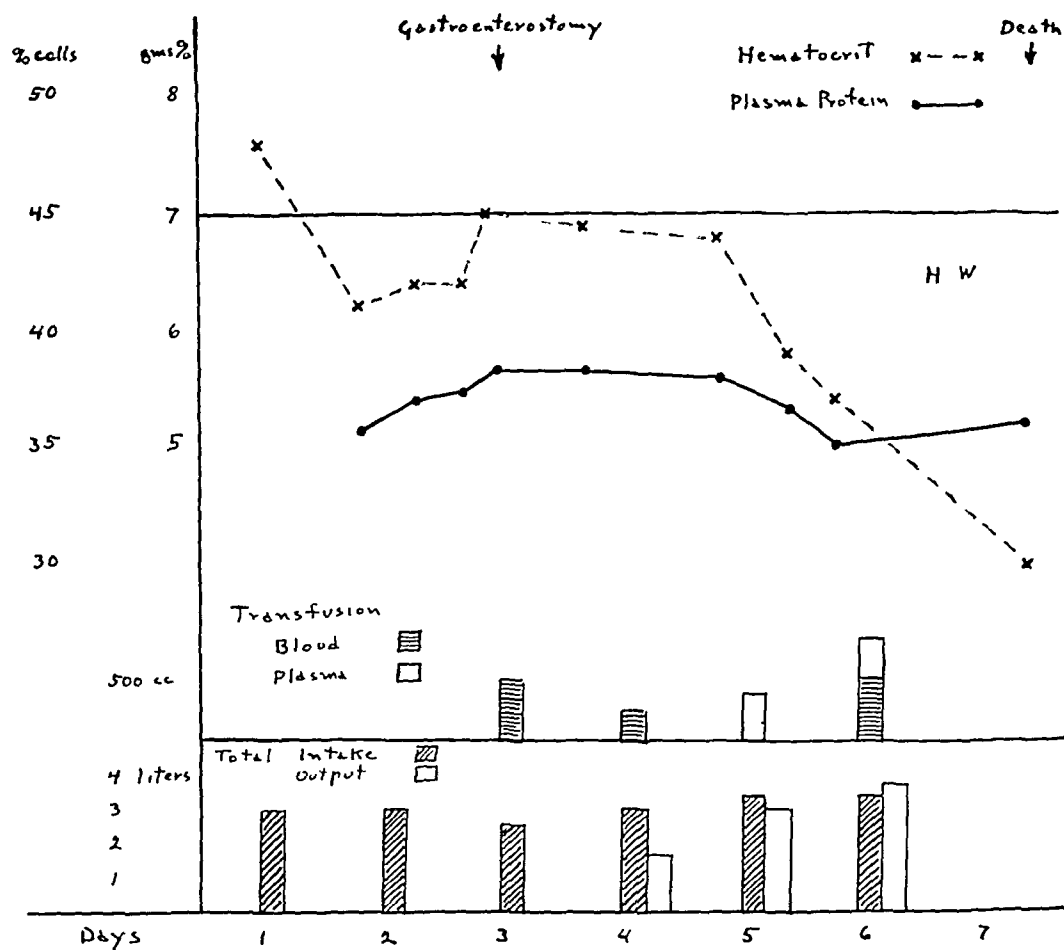


CHART 8—Case 7. Illustrates the occult hemorrhage revealed by the falling hematocrit while the protein level was being maintained. Hemorrhage was subsequently confirmed by tarry stools.

Every patient was an individual problem, and, while the general trend of values followed the types shown in Chart 1, the time relations and magnitude of changes varied from patient to patient. The particular determinations made on a given patient depended upon the physiologic problem involved, and the kind and quantity of parenteral medication had to be redetermined at frequent intervals.

There seems to be some justification in presenting another formula for calculating electrolyte requirement. The emphasis should be shifted from neutral salt to total base, which is the factor that determines the amount of water held in the tissues. Analyses will indicate the appropriate acid ion,

bicarbonate, chloride, or lactate, for balancing the base given. Formulae proposed by other authors have neglected the factor of hemoconcentration, not only as an indicator, in itself, of loss of extracellular water, but as a clue to loss of extracellular base not shown by plasma electrolyte concentrations. Even with this correction the formula (as with those proposed by others) suffers from the fact that the actual or optimal volume of the interstitial reservoir is not accurately known. For practical purposes our calculations

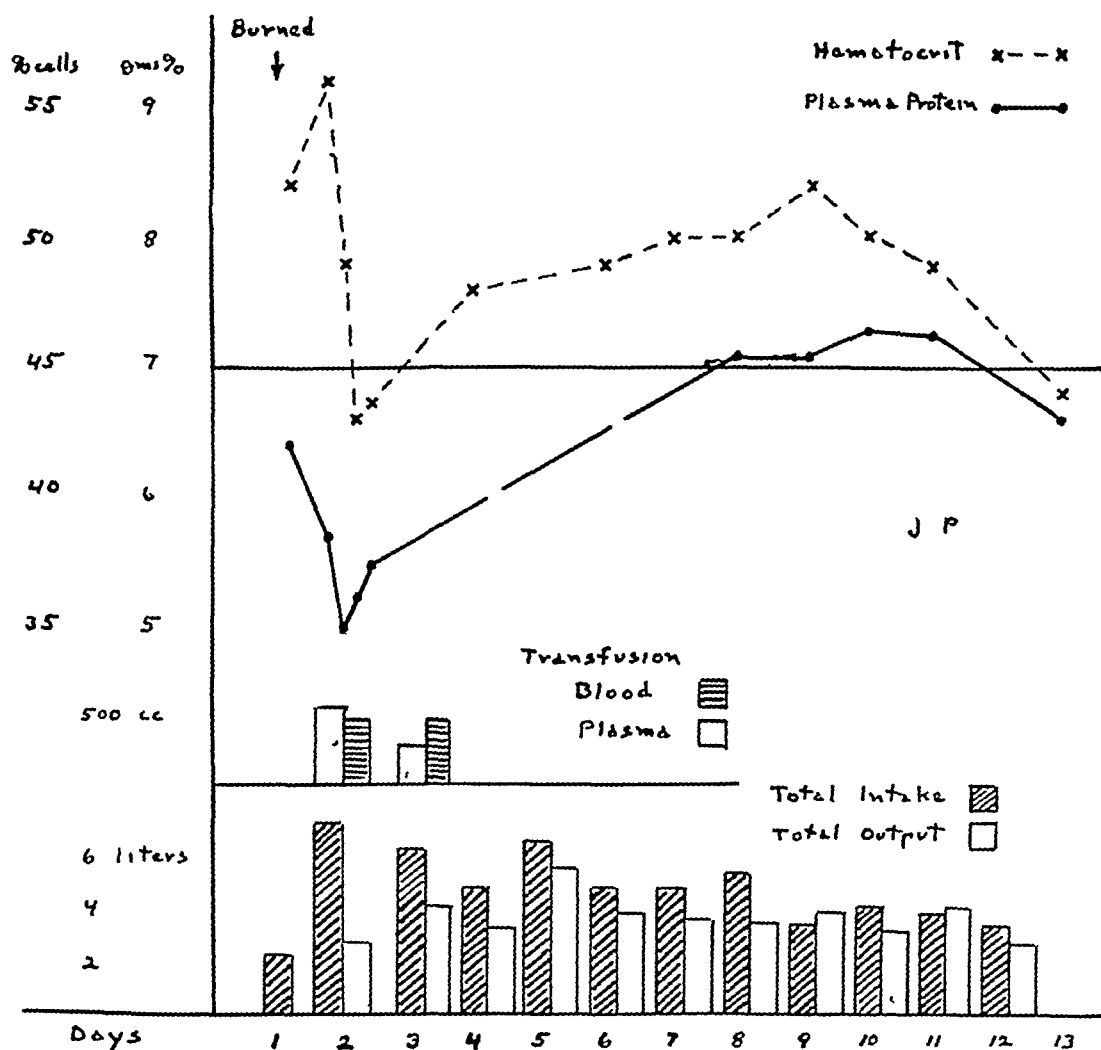


CHART 9—Case 8 Shows

- (1) The early marked loss of protein at the same time that the blood is rapidly concentrating—a prime indication for plasma transfusion
- (2) The response to therapy evidenced by hemodilution and rise of the plasma protein level
- (3) The severe systemic disturbance that may follow a relatively small burned area

have been based on the assumption that total extracellular fluid volume amounts to 20 per cent of the body weight. However, the use of these approximate calculated values marks an advance over arbitrary rules so prevalent in the early days of parenteral therapy.

Unavoidable difficulties arise in the control of water and electrolyte balance in patients with anemia, hypoproteinemia, and cardiovascular or renal disease. Although establishing a base-line in patients with a deficiency of erythrocytes or plasma protein is merely a guess, serial determinations in this type of patient

are valid. In patients with cardiovascular disease the route and rate of parenteral administration of fluids must be modified in order to avoid circulatory embarrassment. The damaged kidney, in many instances, is unable to conserve base and eliminate acid ions preferentially, or to handle large quantities of electrolytes. In those patients with low levels of plasma protein, the administration of the calculated quantity of electrolyte may produce edema.

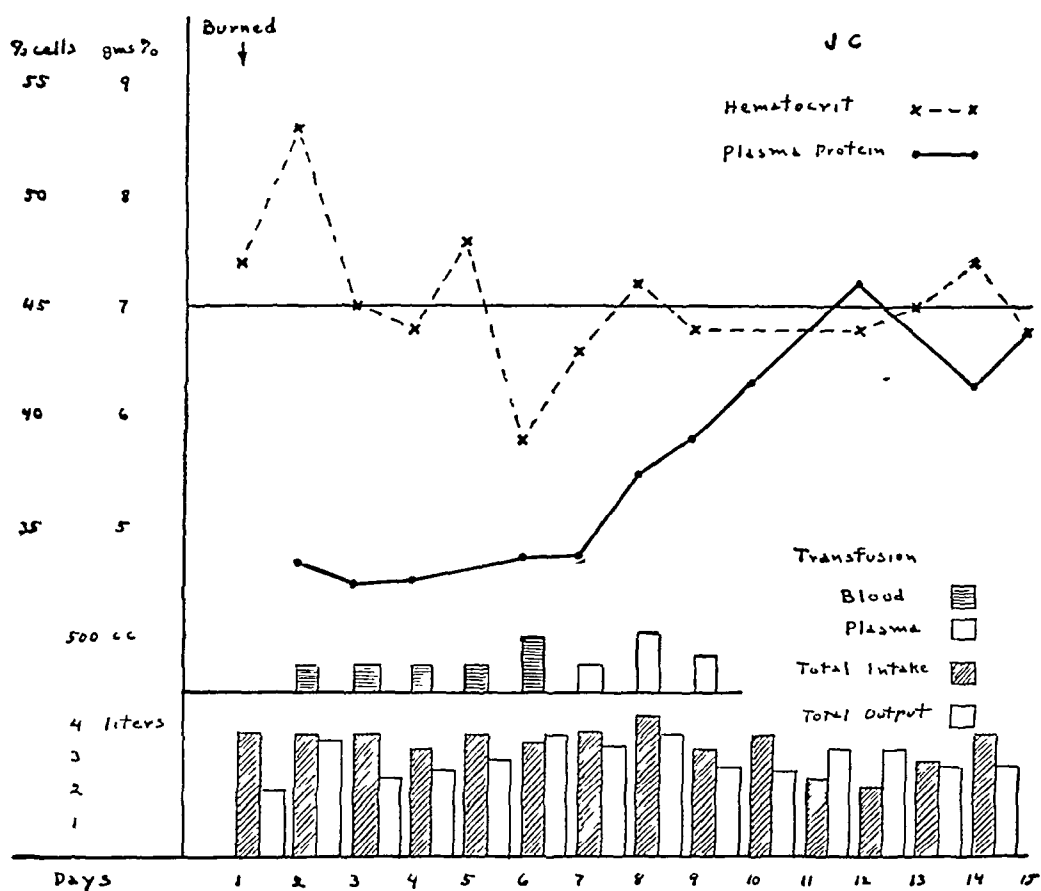


CHART 10—Case 9 Shows

- (1) The early hemoconcentration with the marked loss of protein
- (2) The rise in plasma protein following the initiation of plasma transfusions

Furthermore, patients losing large amounts of protein through the kidney seldom benefit from plasma transfusion.

CONCLUSIONS

Electrolyte and water balance in surgical patients may be evaluated fairly accurately by simultaneous determinations of hematocrit value, plasma protein, chlorides, and carbon dioxide combining power. From the two latter figures the total base is approximated. Hemoconcentration, as shown by a rising hematocrit or plasma protein value, is an indication of serious depletion of the extracellular water. A falling total base concentration indicates serious extracellular base depletion, and, when corrected for hemoconcentration, may be used to calculate the amount of base required.

The analytic results also indicate the type of parenteral fluid needed, either whole blood, plasma, physiologic saline, bicarbonate and lactate, or glucose in distilled water. Such a routine has been found valuable in those patients presenting serious problems of fluid balance.

The authors wish to thank Dr. Walter E. Lee and Dr. John B. Flick for their encouragement and for access to the patients on their Services, and to acknowledge the assistance of Miss Marian Janney, and of the hospital clinical and laboratory staffs. The

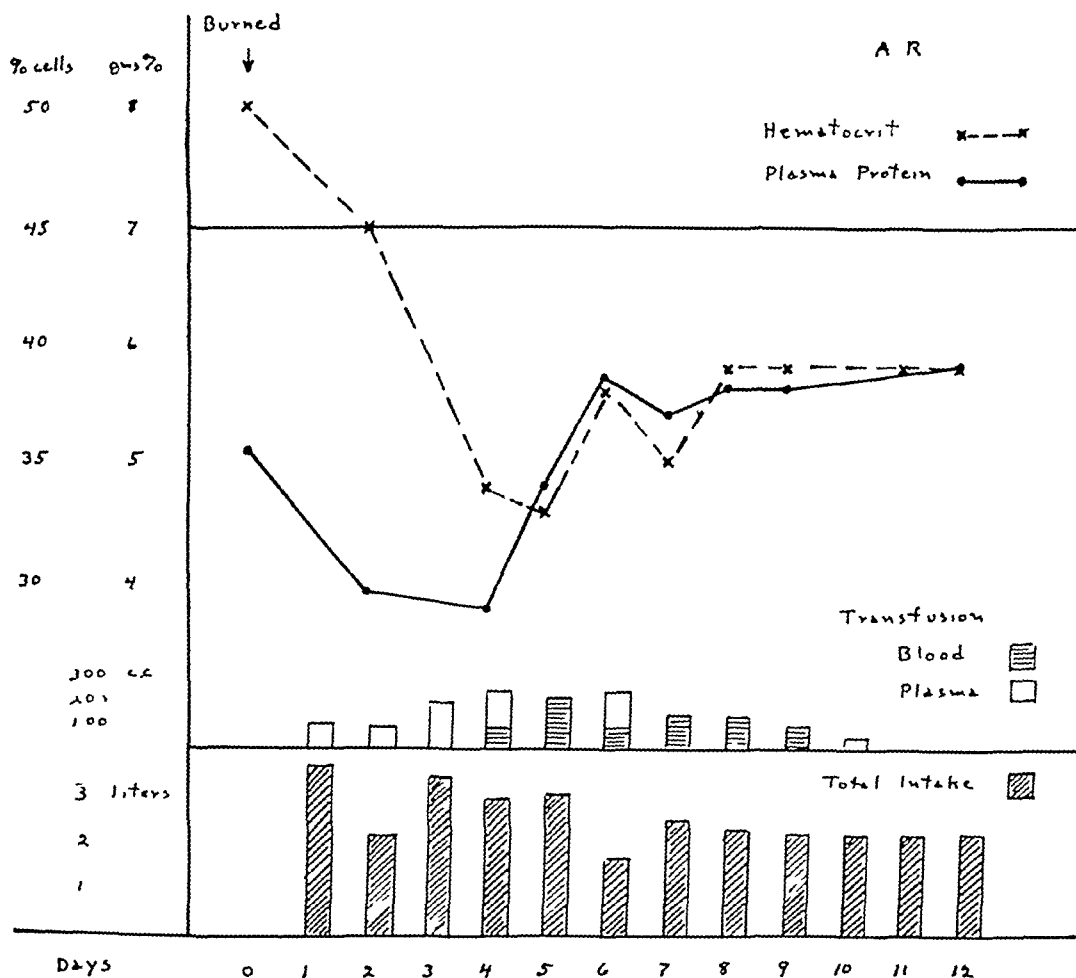


CHART 11—Case 10 Shows

- (1) The very marked protein loss in the presence of hemoconcentration
- (2) The hemodilution in response to plasma transfusions and parenteral fluid with maintenance of the protein level
- (3) The substitution of blood for plasma when the hematocrit fell well below normal, and a satisfactory response in hematocrit level

authors are also indebted to Drs. John Scudder and C. R. Drew of Presbyterian Hospital, New York City, for demonstrating the hematocrit and plasma protein methods and results on their patients.

REFERENCES

- ¹ O'Shaughnessy. Letter to London Medical Gazette 9, 486, 1831-1832
- ^{2a} Peters, J. P. Body Water. Charles C. Thomas, Springfield, Ill., 1935
- ^{2b} *Idem*, Chap. III
- ^{2c} *Idem*, Chap. VI
- ³ Collier, F. A., Bartlett, R. M., Bingham, D. L. C., Maddock, W. G., and Pedersen, S. The Replacement of Sodium Chloride in Surgical Patients. *ANNALS OF SURGERY* 108, 769, 1938

- ^{3a} Bartlett, R M , Bingham, D L C , and Pedersen, S Salt Balance in Surgical Patients Surgery, 4, 441, 614, 1938
- ⁴ Stewart, J D Fluid Therapy in Surgery A Critical Review New England Jour Med , 215, 53, 1936
- ⁵ Fantus, B Fluid Postoperatively A Statistical Study J A M A , 107, 14, 1936
- ⁶ Standard, S Water and Salt Metabolism Internat Abstr Surg , 67, 301, 1938, in Surg, Gynec & Obstet, October, 1938
- ⁷ Scudder, J , Drew, C R , and Sloan, L W Anhydremia in Appendicitis Surg Clin North Amer , 19, 295-306, 1939
- ⁸ Gamble, J L Dehydration New England Jour Med , 201, 909, 1929
- ⁹ Cannon, W B Organization for Physiological Homeostasis Physiol Rev , 9, 399, 1929
- ¹⁰ Laviates, P H , Bourdillon, J , and Klinghoffer, K The Volume of Extracellular Fluids of the Body Jour Clin Invest , 15, 261 1936
- ¹¹ Gamble, J L , and McIver, M A Body Fluid Changes Due to Continued Loss of the External Secretion of the Pancreas J Exper Med , 48, 859, 1928
- ¹² Keith, N M Experimental Dehydration—Changes in Blood Composition and Body Temperature Amer Jour Physiol , 68, 80, 1924
- ¹³ McIver, M A , and Gamble, J L Body Fluid Changes Due to Upper Intestinal Obstruction J A M A , 91, 1589, 1928
- ¹⁴ Van Slyke, D D , Wu, H , and McLean, F C Studies of Gas and Electrolyte Equilibria in the Blood V Factors Controlling the Electrolyte and Water Distribution in the Blood Jour Biol Chem , 56, 765, 1923
- ^{15a} Peters, J P , and Van Slyke, D D Quantitative Clinical Chemistry Interpretations, 761 Williams and Wilkins Co , Baltimore, 1931
- ^{15b} *Idem*, 780
- ¹⁶ Moore, N S , Van Slyke, D D The Relationships between Plasma Specific Gravity, Plasma Protein Content and Edema in Nephritis Jour Clin Invest , 8, 337, 1929-1930
- ¹⁷ Thompson, W D , Ravdin, I S , and Frank, I L Effect of Hypoproteinemia on Wound Disruption Arch Surg , 36, 500, 1938
- ^{17a} Thompson, W D , Ravdin, I S , Rhoades, J E , and Frank, I L Use of Lyophile Plasma in Correction of Hypoproteinemia and Prevention of Wound Disruption Arch Surg , 36, 509, 1938
- ¹⁸ Barbour, H G , Hamilton, W F The Falling Drop Method for Determining Specific Gravity Jour Biol Chem , 69, 625, 1926
- ¹⁹ Gamble, J L Chemical Anatomy, Physiology and Pathology of Extracellular Fluid A Syllabus Department of Pediatrics, Harvard Medical School, Boston, 1939
- ²⁰ Butler, A M Electrolyte and Water Balance New England Jour Med , 220, 827, 1939
- ²¹ Elman, R , and Weiner, D O Intravenous Alimentation with Special Reference to Protein (Amino Acid) Metabolism J A M A , 112, 796, 1939
- ²² Hartmann, A F , and Senn, M J E Studies in the Metabolism of Sodium r-Lactate II Response of Human Subjects with Acidosis to the Intravenous Injection of Sodium r-Lactate Jour Clin Invest , 11, 337, 1932

THE COMBINED USE OF ZINC PEROXIDE AND SULFANIL-AMIDE IN THE TREATMENT OF CHRONIC, UNDER-MINING, BURROWING ULCERS DUE TO THE MICRO-AEROPHILIC HEMOLYTIC STREPTOCOCCUS*

FRANK L. MELENEY, M.D., AND HAROLD D. HARVEY, M.D.
NEW YORK, N. Y.

FROM THE BACTERIOLOGICAL RESEARCH LABORATORY OF THE DEPARTMENT OF SURGERY, COLUMBIA UNIVERSITY, AND THE SURGICAL SERVICE OF THE PRESBYTERIAN HOSPITAL, NEW YORK, N. Y.

THE SUCCESSFUL treatment of chronic undermining, burrowing ulcers with zinc peroxide has been reported in four previous communications^{1,2,3,4} and has been confirmed by several other authors^{5,6,7}. These infections are being seen and recognized with increasing frequency, but there is still undue delay in their diagnosis and in the institution of proper treatment. The



FIG. 1—Case 1—on admission. Note the extensive undermining of the skin and in between the femur and the hamstring muscles. The saphenous vein is intact but thrombosed. There is no gangrene of the skin. There is an almost 90° contracture of the knee.

chronicity as well as the extent of these extraordinary defects in the surface of the body renders them certain to be contaminated with many different species of bacteria. Some of these organisms are mere contaminants and are present in small numbers only. Others find the surface exudate suitable for rapid multiplication, but they do not penetrate the tissues. Still others are able to invade the deeper tissues of the body and take part in the infection.

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1930.

itself. For these reasons, a number of different organisms which have frequently been found to be associated with these ulcers have been considered



FIG 2—Case 1—19 days after excision and before skin graft. New epithelium is growing in at the margins. The cavity beneath the femur is smaller. An attempt was made to save a skin flap for the groin, but this was not worth while. No activity of infection developed at the site of ligation of the sphenous vein near the femoral



FIG 3—Case 1—26 days after excision, seven days after skin graft. Some of the grafts have fused with each other and with the marginal epithelium.

the etiologic agents when the really significant organism has not been obtained on culture. The essential organism has frequently been missed simply

ZINC PEROXIDE AND SULFANILAMIDE

because, in the great majority of hospitals, bacteriologic studies are limited to simple aerobic cultivation on routine media

We have had the opportunity of studying over 40 of these unusual infections. By careful anaerobic as well as aerobic studies, we have invariably

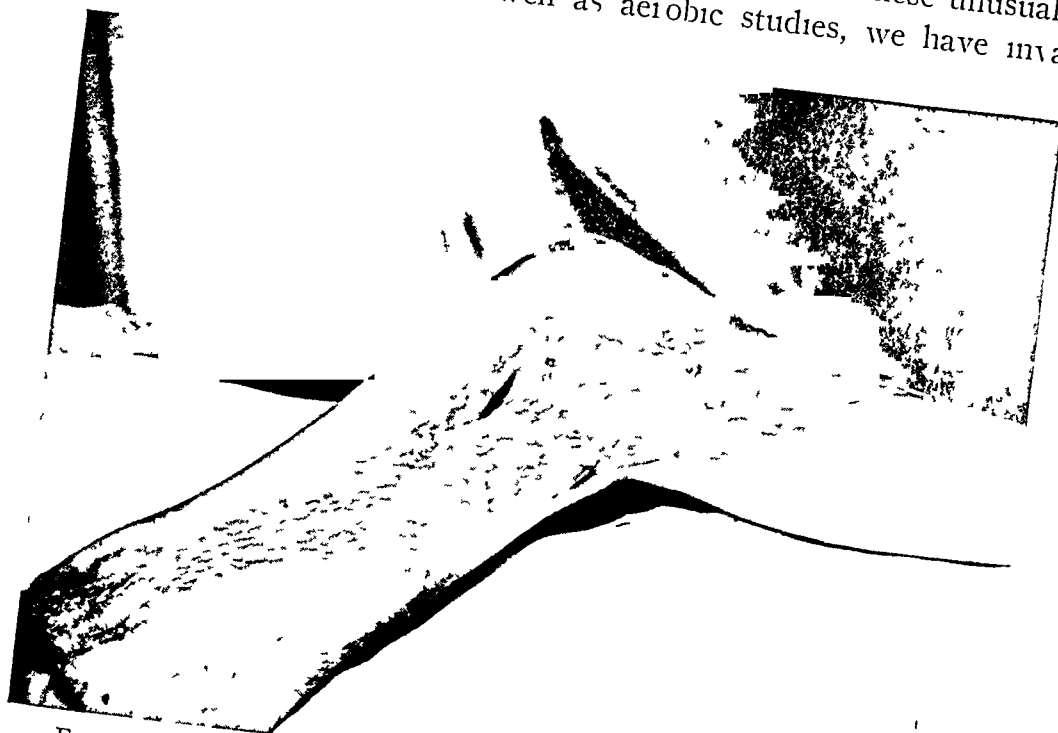


FIG 4—Case 1—45 days after excision, 26 days after skin graft. The area is almost covered with epithelium. The cavity beneath the femur is smaller. Extension of the knee approximates 135° . Extension

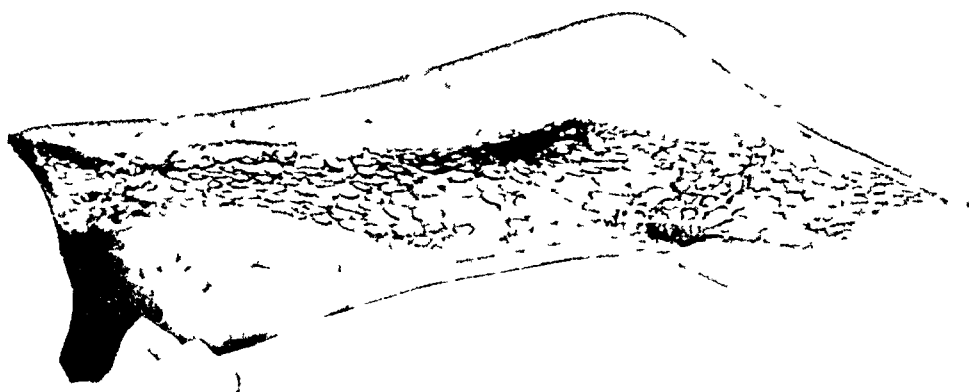


FIG 5—Case 1—80 days after excision, 10 days after complete healing. Extension of leg is about 150° . Extension

found the micro-aerophilic hemolytic streptococcus to be present. In many instances, it has been found in pure culture, when specimens of exudate have been taken from the deep sinuses or from far beneath the undermined skin



FIG 6—Case 2—just before operation. Note the ulceration extending over but not exposing the thyroid cartilage. Undermining extends down to the clavicle and up to the mandible. Lymph nodes on the jugular vein at the angle of the jaw and in the tip of the parotid were involved and were removed.



FIG 7—Case 2—late result seven months after complete healing. The only Thiersch graft case in the series. The skin moves freely over the thyroid cartilage and movements of the neck are only slightly restricted.



FIG. 8—Case 4—on admission. Note the shaggy base of the ulcer on the arm and the extensive undermining with daughter ulcerations forming as perforations from beneath. The axillary ulcer is smaller though older and two sinuses extend upward to the lymph nodes. No gross connection could be found between these ulcers and the arm lesion may have resulted from inoculation of the surface.



FIG. 9—Case 4—three months after excision one month after complete healing. Abduction of arm only slightly limited. Skin soft and pliable.



FIG. 10—Case 6—on admission about two weeks after zinc peroxide had been used. It is obvious that adequate contact was not possible in certain areas. A skin bridge between a daughter ulcer and the main ulcer is shown. A skin bridge had been left but curled up and there is active infection of the base.



FIG 11—Case 6—on admission. Note the skin bridges and the rolled in, undermined margins

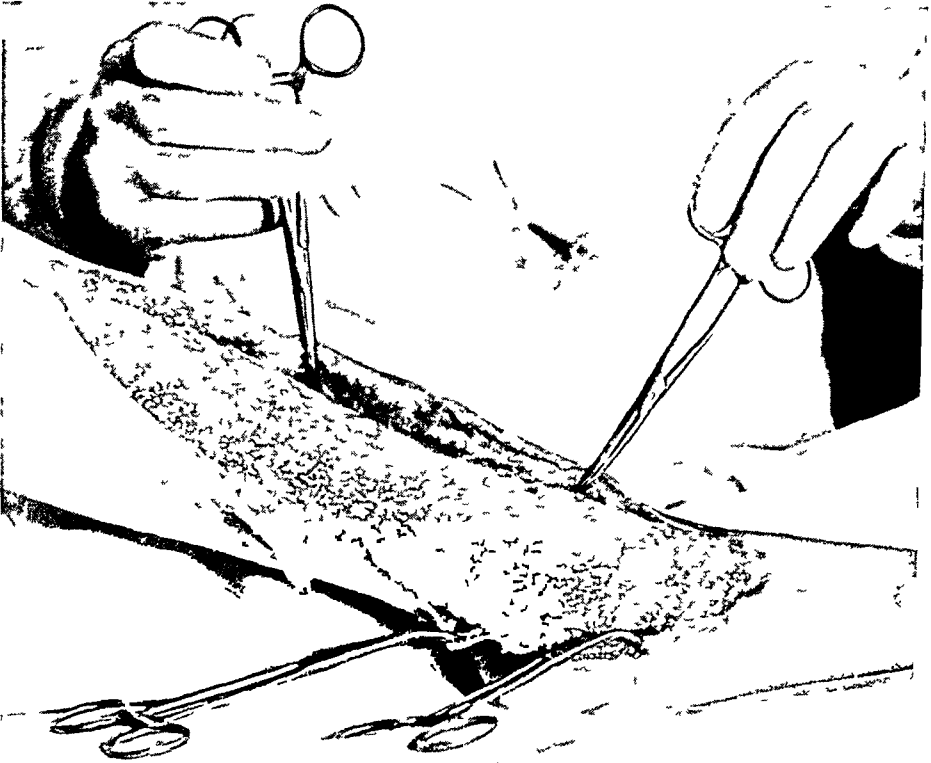


FIG 12—Case 6—on admission. The flaps are extensively undermined. The tip of the upper clamp enters a small perforation of the skin from beneath. There are two other areas of activity below where adequate contact had not been possible

flaps where the inflammatory process is often most active. On certain occasions, also, during the course of treatment, when the organisms have been largely removed from the wound, some little area of recurrent activity has

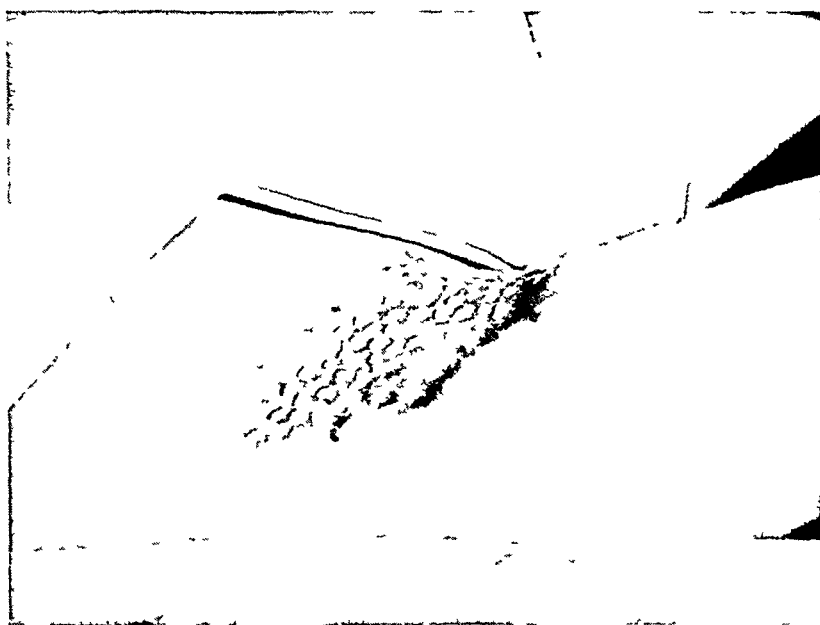


FIG 13—Case 6 Healing complete 39 days after excision and 29 days after skin graft. There had been a little mechanical erosion of the marginal epithelium which promptly healed over.

shown the reactivation or persistence of this organism. Therefore, even though we have not been able to produce this disease in animals and thus fulfill Koch's postulates for the final proof of etiology, we feel confident that

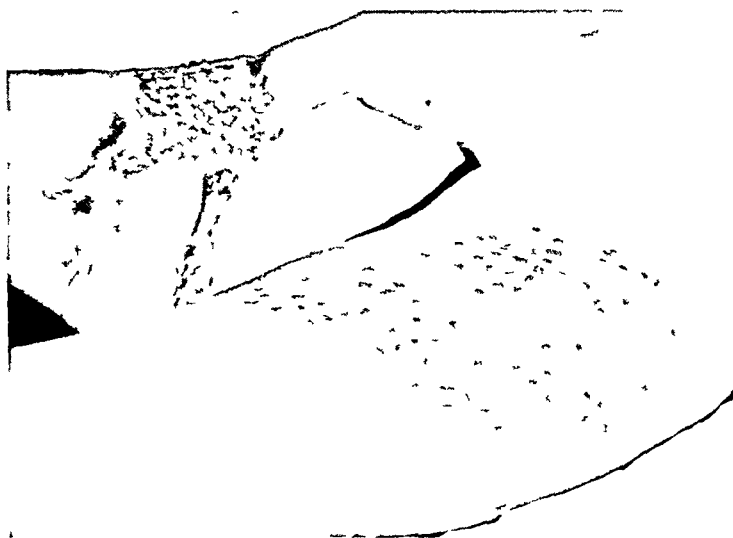


FIG 14—Case 6—time same as in Figure 13. Healing complete of donating and receiving areas.

its invariable presence at times in pure culture establishes it as the etiologic agent for this clinical entity, and we believe that the failure of others to find this organism in these lesions can be traced to faulty or inadequate methods of bacterial cultivation.

Laboratory studies with these organisms have shown them to be micro-

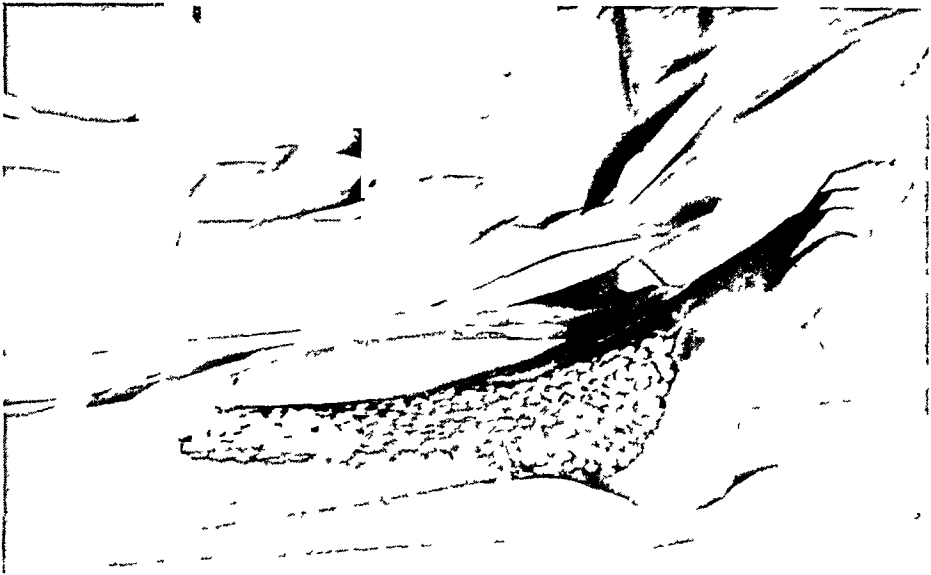


FIG 15—Case 6—time same as in Figure 14. Healing of leg complete. There is a slight degree of foot drop.

aerophilic hemolytic streptococci lying intermediate between the aerobic hemolytic streptococci and the strictly anaerobic hemolytic streptococci, pre-

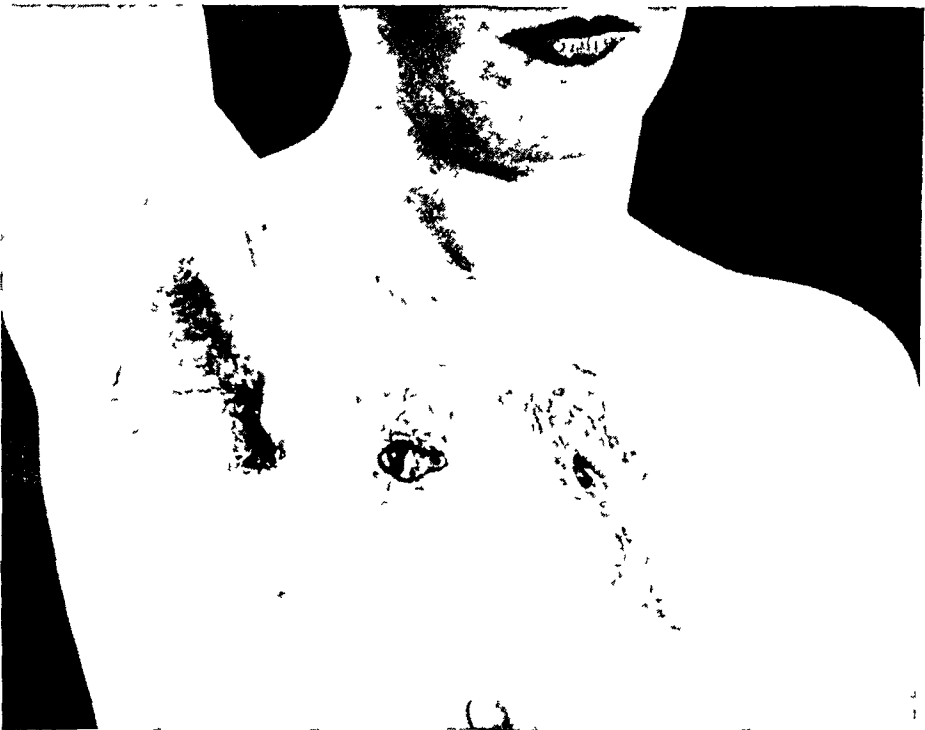


FIG 16—Case 14—on admission. Note the relatively small ulceration in the neck. Two sinuses have burrowed through the pectoral muscles from beneath.

ferring for their multiplication a reduced oxidation-reduction potential in their environment. When they are in this state, they have certain under-



FIG 17—Case 14—three days after complete excision of the diseased tissue. Zinc peroxide is adherent to freshly cut surface. No repair as yet. Patient prostrated by high temperature and in delirium both of which ceased on withdrawal of sulfanilamide.



FIG 18—Case 14—20 days after excision just before skin graft. Good granulating surface. Edges are adherent and new epithelium is growing in.

mining burrowing propensities, which may be linked up with their preference for a partially anaerobic environment. After a few transplantations on artificial media, these organisms can be made to grow readily under ordinary aerobic conditions. When this has occurred the usual tests applied for the

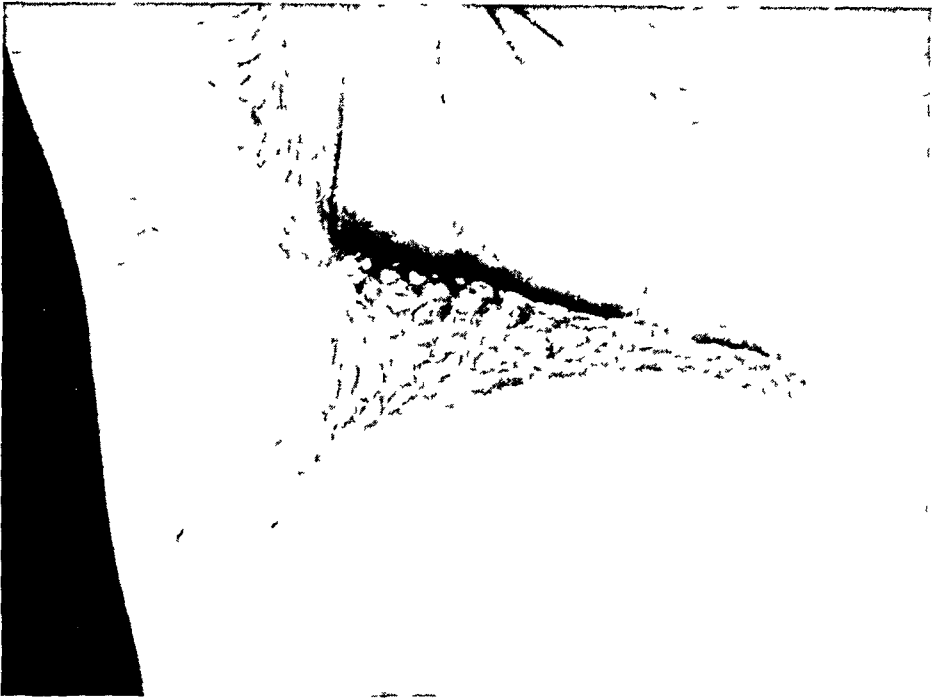


FIG 19—Case 14—41 days after excision, 12 days after skin graft Healing complete
Abduction of arm only slightly limited



FIG 20—Case 15—on admission Chronic infection of 19 years' standing has resulted in redundant folds of skin overlying a maze of sinus tracts undermining the skin and extending up to axillary nodes

differentiation and classification of hemolytic streptococci do not show any significant differences between these organisms and aerobic hemolytic streptococci obtained from other human lesions All that we have tested fall into

Lancefield's⁸ Group A and into heterogeneous groups according to fermentation reactions or agglutination tests

For this reason, when sulfanilamide was found to act favorably in ordinary hemolytic streptococcus infections, this drug was applied in instances of



FIG 21—Case 15—on admission. A condition similar to that involving the axilla in the right groin and scrotum

these lesions also. Sometimes this drug has been used in the treatment of these cases by doctors who have not taken the trouble, or have not had the facilities, to make bacteriologic studies. We have attempted to employ it in the treatment of the last 20 cases, which have come under our care after thorough bacteriologic studies had been made. In these cases, we have used sulfanilamide either alone or in conjunction with zinc peroxide.

The use of zinc peroxide has certain disadvantages because its activity



FIG 22—Case 15—13 months after final healing which was complete in seven weeks after operation. Right axilla. Cavity lined with epithelium. Scar somewhat keloidal—softened by radiotherapy. Abduction only slightly limited.



FIG 23—Case 15. Left axilla of case shown in Figure 22.



FIG 24—Case 15. Thirteen months after final healing of perineum which was complete seven weeks after operation.

depends upon its close application to the infected tissues. These may be deep under skin flaps or deep down in sinuses or in the center of lymph nodes. In most cases, this requires a preliminary surgical procedure, in order to expose these tissues in such a manner that the zinc peroxide can be properly applied. It would obviously be of great advantage if some medication could be introduced into the body through the circulation, which would reach the advancing margin of the infection either under the skin or deep down in the tissues.

Sulfanilamide acts most dramatically in the early stages of an acute infection caused by the hemolytic streptococcus where there is a condition of cellulitis without any necrosis of tissue, where the blood supply has not been shut off by thrombosed blood vessels and where the drug can diffuse out into the tissues and come in close contact with the organisms. Where there has been a necrosis of tissue or abscess formation,



FIG 25—Case 16—on admission. Note the relatively limited undermining. However, the degree of induration around the lesion prevents adequate contact by zinc peroxide without preliminary excision.



FIG 26—Case 17—29 days after excision, 18 days after skin graft. Epithelialization is complete. The new epithelium is cyanotic from too rapid dependency, which should have been avoided.

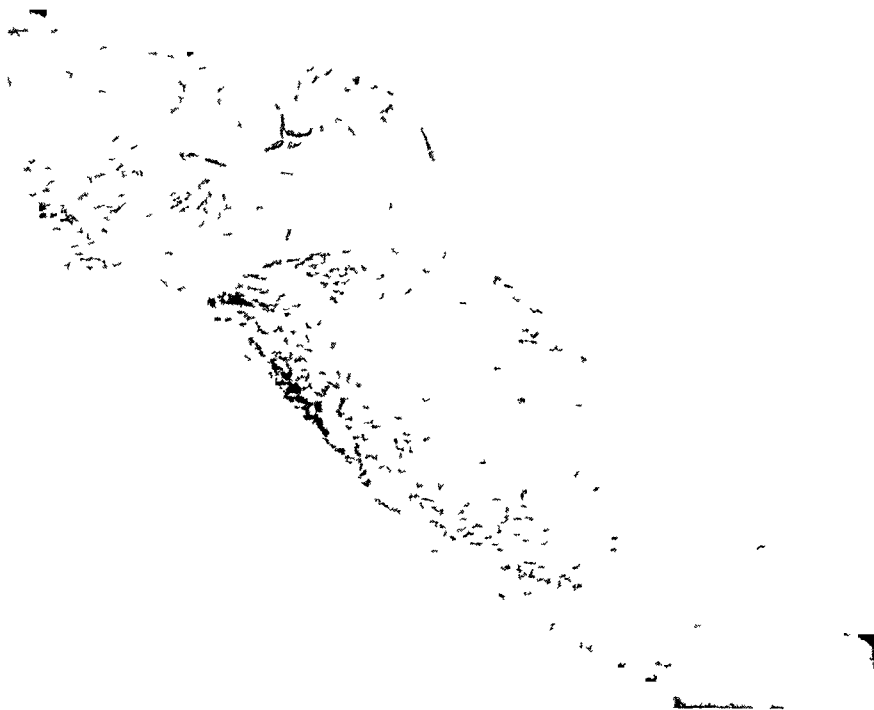


FIG 27—Case 17 Six months after complete healing

the curative effect with sulfanilamide is definitely limited and surgical drainage with liquefaction and removal of the dead tissue is required before healing can take place



FIG 28—Case 19—on admission Breast is completely undermined and hanging by two pedicles, with an ulcer in between and on either side

Lockwood,⁹ in 1938, reported his experiences with sulfanilamide in hemolytic streptococcus infections and showed that the presence of peptones markedly interfered with the bactericidal action of sulfanilamide on the hemo-



FIG 29—Case 19 One month after final healing, which was accomplished in four months



FIG 30—Case 20—on admission. Note the relatively small ulceration. There is extensive undermining and induration with multiple cribriform sinus openings

lytic streptococcus. This may explain the relative inefficiency of the drug in chronic streptococcus infections and in the late stages of acute or subacute infections when there is a considerable amount of necrotic tissue in which the split products of protein, such as peptones, are present in large amounts. Swift,¹⁰ *et al* have found that sulfanilamide has not been effective in rheumatic fever and other subacute or chronic streptococcus infections and that toxic manifestations are more frequent in these cases. Recent work by Fox¹¹ *et al* on sulfanilamide from the viewpoint of oxidation-reduction potentials of

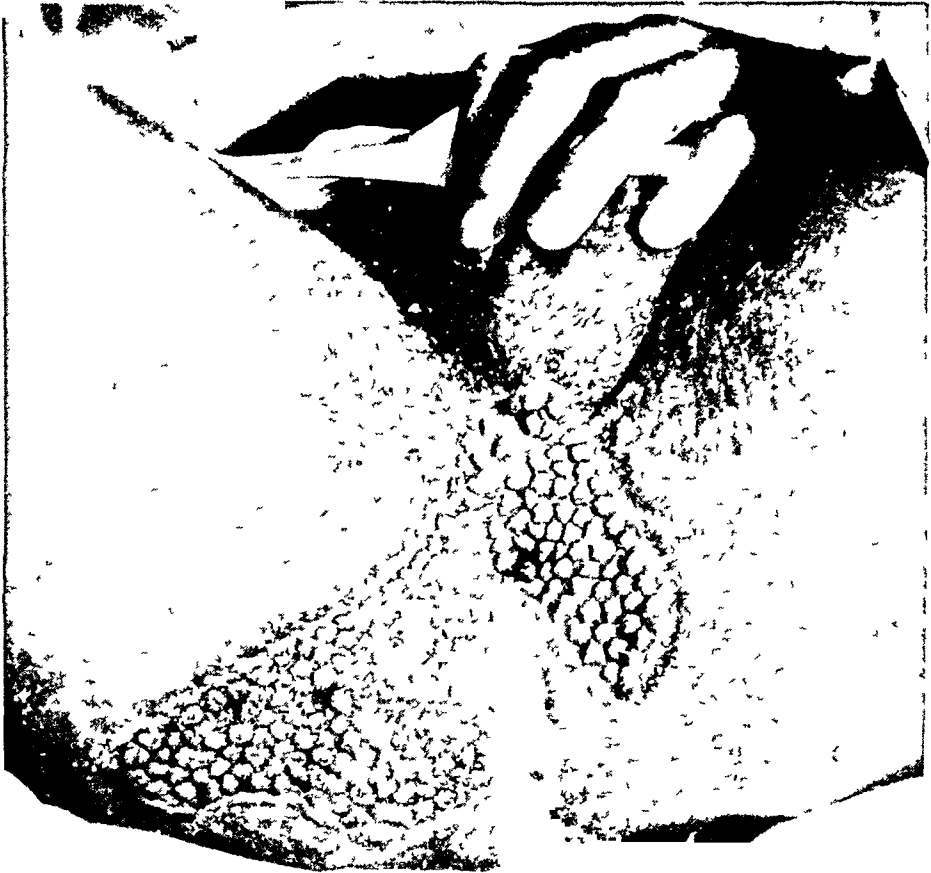


FIG. 31—Case 20—21 days after excision two days after skin grafting. All but two or three grafts have become adherent.

the environment and the electrical reactions of streptococci suggests that a lowering of the oxidation-reduction potentials towards anaerobic conditions or the lowering of the iso-electric point of the bacteria may interfere with the bactericidal action of sulfanilamide. It is to be expected, therefore, that there might be limitations or difficulties in the administration of sulfanilamide in cases of undermining, burrowing ulcer.

However theoretical these considerations may be, it was only by practical experience that the relative value of these two drugs could be determined, and the steadily increasing number of the cases that have come under our observation in the last few years has given us an unusual opportunity for this study.

The 20 cases included in this report do not differ fundamentally from those previously described. They fall into the three main groups (1) Post-operative, (2) lymph node involvement, and (3) secondary contamination of an accidental wound or a previously existing infection. Our experience with these cases has confirmed our previously stated opinion that the organism is a hemolytic streptococcus, which has become adapted to an anaerobic



FIG 32—Case 20 Six months after final healing

environment either while residing in the intestinal tract or vagina of the patient or while smoldering in a lymph node.

Each case has certain features of its own and at the same time shows the fundamental characteristics of the disease entity. In certain areas where the skin is thick and probably resistant to necrosis, the burrowing propensities of the organism outweigh the ulcerating propensities. These regions are the perineum and buttocks, vulva, scrotum and axillae. Here multiple sinuses are common and ulceration is generally limited.

The secret of success with zinc peroxide depends upon three fundamental requirements, and the treatment of the cases which have come to us from other doctors who have employed zinc peroxide unsuccessfully has been at fault in

one of these three categories. The first is the material itself. The Du Pont Chemical Company, which manufactured the zinc peroxide originally used and found to be effective, has been the only chemical company consistently able to manufacture effective material. The Merck and Mallinckrodt Companies have tried to do so, but have failed and are now planning to distribute the Du Pont product under its distinctive name, "Z P O". A number of doctors who have attempted to use zinc peroxide in the treatment of these ulcers, even among our own acquaintances, have simply asked their pharmacies to obtain some zinc peroxide without specifying the source. They have then been given either the Merck or Mallinckrodt material and have used it without obtaining satisfactory results. The importance of certain physical properties of this material are of fundamental importance because while the chemical content of zinc peroxide in the powder may be high, the oxygen may not be mobilized or made available. The preliminary heating in a dry oven at 140°C for four hours not only sterilizes the powder, but mobilizes the oxygen. When added to sterile distilled water, after the sterilization and activation process, effective material always flocculates quickly as a soft, curdy mass, leaving a clear supernatant fluid, and it is soon lifted up by the formation of oxygen bubbles. This test should always be made before using any particular preparation.

The second most important feature of the treatment is to obtain close contact between the zinc peroxide and the infection. With many of these ulcers, there are deep, undermined skin flaps and deep sinuses which prevent close contact of the medication unless there has been a preliminary operative procedure undertaken in order to expose the advancing margins of the infection. In many cases, it is obvious when the patient first comes to the doctor that this must be done and it should be done without delay. In other cases, where there is no obvious necrosis of the subcutaneous tissue or induration of the margin, it may be wise to treat the lesion conservatively for a period of a week or ten days. At the end of that time, it will be clear whether or not adequate contact with the material has been obtained, because in those areas where adequate contact has been made, bright red granulations will grow up and if the margin is attached new epithelium will grow in. In those areas where there is no subsidence of the infection or evidence of repair, it is reasonably certain that the zinc peroxide is not coming into adequate contact and these areas must be exposed or excised.

The third essential feature of the treatment is the prevention of evaporation. The oxygen is conveyed from the zinc peroxide to the tissue by means of water. When zinc peroxide is suspended in water, oxygen is given off into the water, hydrogen peroxide is formed and the oxygen is then transferred to the environment. This leaves H_2O , which then takes up more oxygen from the zinc peroxide. If the zinc peroxide dressing is allowed to dry, this action stops or is greatly diminished and the dry material may mechanically irritate the wound whenever the patient shifts his position. The tissue fluids and the body exudates may act as catalytic agents, but the activity of the zinc peroxide suspension is at its best only when extraneous moisture

is present For that reason, the zinc peroxide must not only be applied to every part of the wound surface, but the wound surface must then be covered with a double layer of fine meshed gauze soaked in the suspension This helps to maintain contact, but must, in turn, be covered by gauze compresses or sheet cotton wet with water The whole dressing is then sealed with vaselined gauze or, better still, gauze impregnated with zinc oxide ointment, which is more impermeable to the air and does not irritate the surrounding skin This impermeable covering should have a wide margin around the wet compresses, so that slight movement of the part will not displace them In leg or forearm ulcerations, it is possible at times to use rubber sheeting to seal the dressing, but this is not practical on other parts of the body

When these three features of the treatment have been carried out, it has been invariably successful and in the last 20 cases there have been no fatalities Of these 20 cases, one received zinc peroxide alone, one received sulfanilamide alone, and the other 18 received both In eight, the sulfanilamide was employed before the zinc peroxide, in eight, in conjunction with zinc peroxide both forms of treatment starting at the same time, and in two after the treatment with the zinc peroxide had been begun

Of eight cases in which sulfanilamide was used before the zinc peroxide there was no evidence whatever of any favorable effect in seven In one case in which we were determined to give sulfanilamide a prolonged trial, there was a temporary improvement, but after several weeks, progress came to a standstill Then the infection became active again even with continued medication

In eight cases, the sulfanilamide and zinc peroxide were begun at the same time In one of these patients in whom the infection had entered through a draining sinus from a tuberculous hip and had then produced extensive superficial ulceration with undermining, because of the impossibility of intimate contact, the zinc peroxide was used for only a brief period Improvement continued with the use of sulfanilamide and the ulcer finally healed leaving, however, the tuberculous sinuses which are still draining, two years later Credit in this case must be given wholly to the sulfanilamide Two other cases in this group were given sulfanilamide along with the zinc peroxide treatment without discomfort and possibly with some benefit Two others took the sulfanilamide for 14 and 19 days, respectively, but asked to have it stopped because of a disturbance of digestion Withdrawing the drug had no effect on the progress of healing In the other three patients of this group the drug was highly toxic, one was delirious for five days the other for four days One of these had to be restrained Reason was restored in both cases promptly after withdrawal of the drug The third was extremely nauseated and ran a high temperature for four days Both symptoms promptly disappeared when the drug was stopped

Of the two remaining cases which received sulfanilamide sometime after the administration of zinc peroxide in one the healing process seemed to show a definite spurt when sulfanilamide was given but it had to be discontinued

tinued after four days because of nausea and anorexia. In the other case, there was induration of the margin which had not been brought under control with the zinc peroxide because the preliminary operative procedure did not permit adequate contact. To obviate further operation, sulfanilamide was tried and the infection then came definitely under control.

Mention should now be made of the control cases—one receiving sulfanilamide alone and the other zinc peroxide alone. The first patient had an ulcer beneath the breast of nine months' standing. Six operations had failed to halt the progress of the infection. Sulfanilamide was started and in six days there was striking improvement. It was discontinued for seven days and the activity of the infection recurred. The drug was readministered with steady improvement and final healing, but it took 20 weeks from the time of admission. The other patient had a lesion of the buttock and perineum involving the anus, of four years' duration. It was excised and zinc peroxide was applied. Skin was grafted on the nineteenth day and it was completely healed in 40 days. When the other 18 cases are considered with them, it may not be far wrong to consider these last two cases as representative of the relative value of these two forms of treatment in chronic, undermining, burrowing ulcer. It is possible for sulfanilamide to result in the healing of certain of these cases without the use of zinc peroxide. This is not only illustrated by one of our cases (Case 19), but it has been reported by others.¹² However, the process of healing was very much longer than in the cases treated with zinc peroxide alone or with a combination of the two forms of treatment.

BRIEF SYNOPSES OF THE 20 CASES TREATED CASES RECEIVING SULFANILAMIDE BEFORE ZINC PEROXIDE

Name Hist No	Location	Type	Duration of Disease	Period of Treatment	Course
Case 1 H K 521 038 Adm 5-28-37 Disch 8-19-37 (Figs 1 2 3 4 and 5)	Leg and thigh	Contam Abscess	6 mos	11 wks	<i>Before admission</i> Multiple boils 2 yrs—one on leg took on new aspect with ulceration undermining up inner surface of thigh to groin. Burrowed beneath bone to outer surface of thigh. Given sulfanilamide. No improvement. Toxic rash. <i>After admission</i> Excision inner aspect. Incision outer aspect. Zinc peroxide. Skin graft.
Case 2 J G 555 200 Adm 8-15-38 Disch 9-26-38 (Figs 6 and 7)	Neck	Lymph node	4 mos	35 das	<i>Before admission</i> Three children had ear infections. Patient developed sore throat and node on right side of neck. Ice bag, ultraviolet light, incision. Sulfanilamide. No improvement. Repeated incisions, ulceration, undermining. <i>After admission</i> Excision. Zinc peroxide. Sulfanilamide intermittently because it upset digestion. Thiersch graft seventeenth day.

ZINC PEROXIDE AND SULFANILAMIDE

BRIEF SYNOPSIS OF THE 20 CASES TREATED (*Continued*) CASES RECEIVING SULFANILAMIDE BEFORE ZINC PEROXIDE (*Continued*)

Name Hist No	Location	Type	Duration of Disease	Period of Treatment	Course
Case 3 H O 397 208 Adm 9-6-38 Disch 10-17-38	Penis and scrotum	Contam Abrasion	2½ yrs	40 das	<i>Before admission</i> Glans penis below meatus became red Washes for 2 mos—no effect Abscess in- cised Cystostomy—open 13 mos Bougies passed Infection flared up Ulceration under penis with undermining extending up over shaft and into scrotum Sulfanil- amide more than 1 mo—no effect <i>After admission</i> Excision Zinc peroxide Skin graft
Case 4 N F 564 285 Adm 10-31-38 Disch 12-30-38	Axilla and arm	Lymph node	8 mos	58 das	<i>Before admission</i> Nurse caring for hemo strep meningitis case No known wound of hand Devel- oped node in left axilla Incised Kept on draining Inoculated onto arm in 2 places Opened and drained Gradually became large ulcer with wide undermining Ultraviolet cod liver oil sulfanilamide 3 wks Toxic for W B C Stopped <i>After admission</i> Excision ulcer Lymphadenectomy Skin graft
Case 5 E N 569 248 Adm 12-26-38 Disch 1-14-39	Leg	Contam Mosquito bite	6 mos	4 wks	<i>Before admission</i> Mosquito bite became infected Incised and later excised Sulfanilamide many weeks—no effect Mercurochrome, car- bolic acid azochloramide alcohol balsam brilliant red and strapping All of no avail <i>After admission</i> Finally excised Zinc peroxide Oxy- quinoline at the last
Case 6 H H 569 335 Adm 12-30-38 Disch 2-13-39 (Figs 8 9 10 11 12 13 14 and 15)	Groin thigh and leg	Lymph node	6 mos	41 das	<i>Before admission</i> Took care of husband with sore throat Developed sore throat herself and then swelling in right groin Sulfanilamide by mouth and prontosil intramuscularly daily for 143 das, mercurochrome dichloramine T and saline locally Scarlet fever anti- toxin 5x Welch antitoxin 2x Transfusions 10x 10% prontosil dressings locally Later alternating gentian violet and mercuro- chrome Vaccine on 144th day After sixth dose developed erysipelas which extended down to leg and foot localizing there Incisions Increased doses of sul- fanilamide Blood level 11 mg per cent Started zinc peroxide, immediate improve- ment but did not get adequate control <i>After admission</i> Excised Zinc peroxide Skin graft teeth day
Case 7 R W Seen and and treated in private o- fice only	Thigh	Lymph node	2 yrs	4 wks	<i>Before admission</i> Splinter in foot became infected increased to 1 1/2 in. Contaminated by dirt Ulcer formed and spread on inner surface of foot <i>After admission</i> Excised Zinc peroxide Skin graft teeth day

BRIEF SYNOPSIS OF THE 20 CASES TREATED (*Continued*)
CASES RECEIVING SULFANILAMIDE BEFORE ZINC PEROXIDE (*Continued*)

Name Hist No	Location	Type	Duration of Disease	Period of Treatment	Course
Case 8 J H 561 802 Adm 9-27-38 Disch 4-1-39	Behind ears, both axillae, scrotum, perineum	Contam Boils	Axillae, peri- neum and groins 6 yrs Ears 8 mos	145 das in hospital	<i>Before admission</i> For years had pimples and boils Infection in groin spread down along scrotum to perineum About same time developed same lesion in axillae 8 mos ago he be- came inoculated behind both ears Many hospitals many opinions many operations Steady spread <i>After admission</i> Sulfanilamide Improvement 2 wks then standstill Gentian violet Cod liver oil Repeated transfusions Infection active again Zinc peroxide Immediate improvement Needed more exposure Too conservative

CASES RECEIVING SULFANILAMIDE WITH ZINC PEROXIDE

Case 9 P M 499 980 Adm 10-3-36 Disch 12-9-36	Hip and thigh	Contam T B sinuses	T B sinus 5½ yrs Ulcer 16 mos	10 wks	<i>Before admission</i> Limped as child of 3 Diagnosed by x-ray as tuberculosis of hip Developed sinus in mid thigh and later one near hip 16 mos ago ulcer developed around sinus—grad- ually spreading extensively <i>After admission</i> Given sulfanilamide and zinc peroxide but after 1 wk latter was stopped because could not get contact Improved steadily with sulfanilamide Grafted
Case 10 J D 548 884 Adm 4-27-38 Disch 5-21-38	Axilla	Lymph node	6 mos	25 das	<i>Before admission</i> Little finger abraded at football Node became swollen in axilla Opened and drained 4x All kinds of antiseptics lo- cally Dakin's mercurochrome maggot fluid Transfusions Ulcer with over- hanging skin flap <i>After admission</i> Zinc peroxide applied Took sulfanilamide without discomfort Rolled in margin cut away Skin graft
Case 11 J T 531 057 Adm 9-27-37 Disch 10-24-37	Perineum and scro- tum	Contam Boils	26 yrs	26 das	<i>Before admission</i> Began with a boil on the right buttock Incision prolonged drainage Repeated operations Never healed Diagnosed T B, but no organisms found (Johns Hop- kins Hosp) Cribriform openings right groin Sinus extending down along scro- tum and up on other side <i>After admission</i> Excision Zinc peroxide Skin graft Sul- fanilamide taken—some nausea
Case 12 C S 446 461 Adm 7-24-38 Disch 10-6-38	Left axilla perineum, abdom wall	Contam Boils	Axilla 12 yrs Perineum and abdom wall 5 yrs	70 das	<i>Before admission</i> Has had pimples for years Sores devel- oped 8 yrs ago in left axilla undermined and formed an ulcer 5 yrs ago infection began on lower abdomen and perineum Diagnosed T B pig negative Frei nega- tive <i>After admission</i> Excision Skin grafts Sulfanilamide 14 das Stopped because it upset digestion Healing delayed by inability to stay quiet after skin grafts

ZINC PEROXIDE AND SULFANILAMIDE

BRIEF SYNOPSES OF THE 20 CASES TREATED (*Continued*)
CASES RECEIVING SULFANILAMIDE WITH ZINC PEROXIDE (*Continued*)

Name Hist No	Location	Type	Duration of Disease	Period of Treatment	Course
Case 13 D K 544 294 Adm 2-21-38 Disch 4-17-38	Thigh	Contam Boil	17 mos	53 das	<i>Before admission</i> Has had multiple pimples and boils for years One took on new aspect with ulceration and undermining Deep sinus formed <i>After admission</i> Excision Zinc peroxide Skin graft Sulfanilamide started at time of operation and given for 19 das Stopped because it upset digestion
Case 14 H S 511 367 Adm 2-23-37 Disch 4-8-37 (Figs 16 17 18 and 19)	Axilla and chest	Lymph node	2 yrs	41 das	<i>Before admission</i> Finger cut by manicure Node swollen in axilla Opened drained Ulcer developed with undermining beneath pectoral muscle which became perforated in 2 places Repeated operations, debridement anti strept vaccines diathermy Autogenous vaccine <i>After admission</i> Excision ulcer, pectoralis cut Zinc peroxide Sulfanilamide High temp and delirium 5 das Fell abruptly on stopping sulfanilamide Skin graft
Case 15 F J 535 644 Adm 11-7-37 Disch 12-21-37 (Figs 20 21 22 23 and 24)	Perineum and both axillae	Post- oper hernia	19 yrs	46 das	<i>Before admission</i> Operated upon for hernia in army in France Wound became infected Spread down along scrotum and up on other side One year later same infection in both axillae Multiple operations Did not heal I B (Peter Bent Brigham Hosp) Never proven <i>After admission</i> Excision Zinc peroxide Sulfanilamide No temp but delirium 4 das Stopped on withdrawal of drug
Case 16 J P 558-089 Adm 3-19-38 Disch 6-30-38 (Fig 25)	Leg	Contam Pimple squeezed	14 mos	38 das	<i>Before admission</i> Started when he picked a pimple on outer side of knee Redness and abscess Opened and drained Did not heal Undermining extended down onto leg <i>After admission</i> Excision Zinc peroxide Skin graft Sulfanilamide High temperature of 104 F for 4 das Stopped on withdrawal of drug

BRIEF SYNOPSSES OF THE 20 CASES TREATED (*Continued*)
CASES RECEIVING SULFANILAMIDE AFTER ZINC PEROXIDE (*Continued*)

Name Hist No	Location	Type	Duration of Disease	Period of Treatment	Course
Case 18 J S 489 587 Adm 6-23-36 Disch 10-28-36	Groin, abdom and thigh	Lymph node	5 mos	4 mos	<i>Before admission</i> Abraded toe Node in groin Incised drained Ulcer formed and spread up on abdomen and down thigh Multiple in- cisions Many antiseptics Strep serum injected around ulcer Injection areas broke down <i>After admission</i> Excision and zinc peroxide Femoral nodes involved Removed piecemeal on several occasions Femoral artery became involved, hemorrhage Artery and vein partially excised Skin graft Prontosil given 4 das with apparent spurt in wound healing Stopped because it upset stom- ach

CASE RECEIVING SULFANILAMIDE ALONE

Case 19 L B 501 444 Adm 10-20-36 Disch 12-24-36 (Figs 28 and 29)	Breast	Contam Pimple	9 mos	20 wks	<i>Before admission</i> Began as a pimple near nipple Abscess developed Incised and drained Con- tinued discharge Finally ulceration began and the whole breast became undermined <i>After admission</i> Sulfanilamide started with improvement in 6 das Stopped with recurrence in 7 das Started again and continued No zinc per- oxide Plastic repair hastened healing
--	--------	------------------	-------	--------	---

CASE RECEIVING ZINC PEROXIDE ALONE

Case 20 W A 546 188 Adm 4-6-38 Disch 5-18-38 (Figs 30 31 and 32)	Perineum and buttocks	Contam Boil	4 yrs	40 das	<i>Before admission</i> Began as boil on side of anus Incised Kept draining Gradually undermined all around anus and out on buttocks with multiple sinuses and cribriform openings <i>After admission</i> Excision Zinc peroxide Skin graft No sulfanilamide
--	-----------------------------	----------------	-------	--------	---

Technic of Treatment—We believe that the ideal treatment of these cases is as follows When the patient first comes to the hospital and after the diagnosis has been made by the clinical appearance of the lesion and confirmed by careful anaerobic as well as aerobic bacteriologic studies, zinc peroxide powder suspended in sterile distilled water in the consistency of 40 per cent cream, should be applied to the wound according to directions mentioned above, due care being taken to use effective material, to get contact and to prevent evaporation This dressing should be removed daily At the same time, sulfanilamide should be administered by mouth, 12 Gm every four to six hours If the patient tolerates the medication and there are no toxic symptoms, such as jaundice, destruction of red cells or white cells, high temperature or delirium, sulfanilamide should be continued If toxic

symptoms supervene, it should be stopped. If after one week there are any areas of activity, one can be sure that an operative procedure is required to permit more adequate contact with the zinc peroxide. Such involved areas should be excised as far as can be done with safety to the life of the patient. Treatment should then continue as before. If there is any evidence of persistent activity after another week's time, further surgical attack should be instituted at once with a wider margin of excision.

It should be well understood that after surgical excision, for the first three or four days, the zinc peroxide is very adherent to the freshly cut surfaces, which have a gray, inert appearance, and it is difficult and unnecessary to wash off this adherent material. One is struck by the absence of inflammatory phenomena such as swelling or pain. Exposed nerves may be painful at first, and after the application of zinc peroxide, for a period of 15 minutes to an hour, there may be an uncomfortable burning sensation. If this occurs, it may be greatly ameliorated by flushing the wound surface with 2 per cent novocain before the reapplication of the zinc peroxide. On the fourth or fifth day, little areas of bright red granulation will appear and these will rapidly increase in size until the whole wound is covered. Then pain and sensitivity completely disappear. As soon as new epithelium grows in from the margin, we are assured that skin grafts will take. In most instances, the small deep grafts are most suitable and there should be almost 100 per cent success. The grafts should be held in place by a single layer of coarse meshed gauze sealed at the skin margin with collodion. They should then be covered with fine meshed gauze wet with saline and cut to the pattern of the wound and then with wet saline compresses and sealed with vaseline or zinc oxide ointment for 24 hours. The following day, the zinc peroxide suspension should be applied over the coarse meshed gauze, gauze compresses or sheet cotton, wet with distilled water, added and the dressing sealed as before. In another 24 hours, the coarse meshed gauze may be removed and the zinc peroxide applied directly to the grafts. All living grafts will be well attached and pink by that time.

As soon as new epithelium begins to grow out from the margins of the grafts, if cultures fail to reveal any viable hemolytic streptococci on anaerobic culture, it is well to change over to 0.5 per cent oxyquinoline in 5 per cent scarlet red ointment which seems to stimulate the rapid growth of epithelium and hasten the final closure of the wound.

REFERENCES

- ¹ Meloney, F. L. Zinc Peroxide in the Treatment of Micro-Aerophilic and Anaerobic Infections. *ANNALS OF SURGERY* 101, 997-1011, 1935.
- ² Meloney, F. L. Zinc Peroxide in Surgical Infections. *Surg. Clin. N. Amer.* 16, 691-711, June, 1936.
- ³ Meloney, F. L. and Johnson, B. A. Further Laboratory and Clinical Experiences in the Treatment of Chronic Undermining Burrowing Ulcers with Zinc Peroxide. *Surgery* 1, 160-221, February, 1937.
- ⁴ Johnson, B. A. and Meloney, F. L. The Antiseptic and Deodorizing Properties of Zinc Peroxide. *Ann. Surg.* 109, 1091-1094, 1939.

- Peroxide on Certain Surgical Aerobic, Anaerobic and Micro-Aerophilic Bacteria
ANNALS OF SURGERY, 109, 881-911, June, 1939
- ⁵ Pennoyer, G P The Value of Zinc Peroxide in the Treatment of Chronic, Undermining, Burrowing Ulcer, Due to the Micro-Aerophilic Hemolytic Streptococcus
ANNALS OF SURGERY, 106, 143-145, July, 1937
- ⁶ Mullen, B P Chronic, Undermining, Burrowing Ulcer of the Abdominal Wall North-west Med, 36, 232, July, 1937
- ⁷ Rhoads, J E The Use of Zinc Peroxide in Micro-Aerophilic Infections Surgery, 2, 937-942, December, 1937
- ⁸ Lancefield, R C The Antigenic Complex of Streptococcus Haemolyticus I Demonstration of Type Specific Substance in Extracts of Streptococcus Haemolyticus
J Exper Med, 47, 91-103, 1928
- ⁹ Lockwood, John S Observations on the Mode of Action of Sulfanilamide and Its Application to Surgical Infections Trans Amer Surg Assoc, 56, 318-324, 1938
- ¹⁰ Swift, Homer F, Moen, Johannes K, and Hirst, George K The Action of Sulfanilamide in Rheumatic Fever JAMA, 110, No 6, 426-434, February, 1938
- ¹¹ Fox, Charles, Jr, German, Bernard, and Janeway, Charles Effect of Sulfanilamide on Electrode-Potential of Hemolytic Streptococcal Cultures Proc Soc Exper Biol and Med, 40, No 2, 184-189, February, 1939
- ¹² Goodman, M H Chronic Streptococcal Ulcer of Skin, Unresponsive to Local Therapy but Cured by Sulfanilamide Report of Two Cases JAMA, 111, 1427-1431, October 15, 1938

DISCUSSION—DR WM BARCLAY PARSONS (New York, N Y) Doctor Meleney is to be congratulated for adding another chapter to his brilliant work on this very important type of infection Doctor Cutler's remarks on surgical training and surgical possibilities, *etc*, are well exemplified in Doctor Meleney's work He has been interested in the symbiosis of organisms and its effect The "symbiosis" of a careful, well-trained surgeon and the bacteriologic laboratory, also, has its very definite effect

We have heard so many enthusiastic reports on the use of sulfanilamide that one can perhaps be pardoned if one takes a little pleasure in hearing a report not too enthusiastic about the use of sulfanilamide, and yet that is not so trivial a point of view as it may seem, because here, there is an attack based upon a very definite set of circumstances, and it is perhaps reasonable, as Doctor Meleney pointed out, that sulfanilamide should not have such a striking success in a chronic, thick-walled, fibrotic, dense area as it would in a fresh, new infection where the drug can be delivered to the organisms

He did not emphasize, as perhaps he might have, although he has emphasized it, I think, in other communications, just that exact point, namely, the delivery of the agent to the organism and the preparation of the wound so that the agent can be delivered to the organism

The first point that he has mentioned as essential to success in this type of treatment, namely, an effective material, is reasonably obvious, and he has mentioned in other papers the difficulties that he has had at times, and which others have likewise had, with an imperfect material

Secondly, the question of absolute contact of the material depends so essentially on the adequate preparation of the wound It is much like the Carrel-Dakin treatment during the war, a good many people said "Oh, that is no good at all," and then it was reasonably obvious that those individuals were not preparing their wounds for the use of the Dakin solution as they should have That is so essential in these wounds, certain examples of which

he has demonstrated. Control of evaporation, of course, is important so that the material can continue to act.

A fourth, and certainly equally important element is the dressing of these cases. Doctor Meleney has never suggested, I think, although I suspect him of feeling it, that the reason for the delay in some of these cases that were handled for weeks and months elsewhere and then came to him and were cleaned up, was the fact that they had not been carefully and properly and thoroughly handled. When he dresses one of these cases, the whole thing is just as though it were a major operation—gowns, gloves, and all the technique that we consider essential to a major operative procedure, and the dressings are done with the most meticulous care. It is advisable during the whole course of the case that these dressings should be done by one man, or at most by two, who are in daily attendance upon that particular patient.

This is a very interesting contribution, and I think it is of real interest that the original scheme which he devised really is the successful one, and that only in a few of the cases does the sulfanilamide act as a helpful adjuvant.

DR ROBERT I. HARRIS (Toronto, Canada). The importance of Doctor Meleney's contribution this morning and those of previous occasions cannot be overestimated. While this condition is rare, the magnitude of the surgical problems it presents is so great that only the principles which Doctor Meleney has laid down have provided us with any means of handling the otherwise insuperable difficulties. Adequate exposure of the wound, the use of an agent which will provide an atmosphere of high oxygen tension over an adequate period of time, and now the use of sulfanilamide are the essential points in treatment.

Doctor Meleney has pointed out that the use of sulfanilamide produces marked improvement, sometimes brilliant results, but that it is not free of difficulties, especially because of its toxicity. It is in this connection that I wish to call to the attention of Doctor Meleney and the fellows of this Association that the concomitant administration of nicotinic acid, in doses of 50 mg. four times a day, reduces the toxic symptoms of sulfanilamide very greatly and frequently eliminates them. In an exceptionally difficult problem of this type which I have had to handle recently, the use of nicotinic acid transformed our problem. This is an empirical use of nicotinic acid for which I am indebted to my medical colleague Dr. Huist Brown.

DR HERMAN E. PEARSE (Rochester, N. Y.). I do not think it is surprising that sulfanilamide does not increase the action of zinc peroxide for zinc peroxide is so efficacious in and of itself. One complication that we have had in the use of this agent is not from the drug itself, but in the preparation of the wound. We have one instance of dissemination of infection with generalized sepsis and metastatic abscess. Under these circumstances, with dissemination of infection, sulfanilamide might be of value. I hope it will not be a digression to mention another use of zinc peroxide. Recently we had a case of Welch bacillus infection in an open wound which could not be cleaned up and the wound could not be healed. Roentgenotherapy, sulfanilamide, and many other local measures were tried. It was then treated with zinc peroxide which resulted in a rapid subsidence of the infection.

of undermining ulcers where we were dealing with an organism, which is micro-aerophilic, that is to say, intermediate between the aerobes and the anaerobes. Naturally, therefore, we applied it at once to the whole series of surgical anaerobic bacteria. In the near future, in the ANNALS OF SURGERY, there will appear a paper which gives our laboratory, and, to some extent, our clinical experiences with anaerobic infections and with the organisms producing them.⁴

The scattering of organisms into the blood stream at the time of operation must be borne in mind, and excessive manipulation of the tissues must be avoided. This complication must be very rare, however, because it occurred in only one of 40 cases which we have seen. This case was included in the second paper of this series. At autopsy, it was found that the patient had a suppurative thrombophlebitis of the common iliac vein.

I am particularly interested to hear of Doctor Harris' experiences with nicotinic acid, and we will certainly take the first opportunity to apply that experience to cases that come to us which show toxicity from sulfanilamide.

Just two other things I would like to add. One is that there is in the literature and perhaps in the minds of some of you, a confusion between two distinct clinical entities exhibiting chronic ulceration. The chronic, undermining, burrowing infection, which I have described and illustrated in the present paper, is characterized by extensive undermining of the skin and burrowing into the deep tissues but without any gangrene. We believe that it is not a symbiotic infection, but caused simply and solely by the micro-aerophilic *hemolytic* streptococcus. Then, there is the symbiotic, progressive gangrenous ulcer, in which there is always gangrene of at least a part of the margin with no undermining of the skin and no deep penetration. If the infection arises from a deep abscess, for example, a pleural or peritoneal abscess, the deep pocket closes and the gangrenous ulcerative process goes on in the skin and subcutaneous tissues in only a very superficial manner, destroying tissue massively as it goes. In that infection, there is another micro-aerophilic organism which is *nonhemolytic* and which can be found out in the periphery in pure culture, and it is always combined with a staphylococcus in the zone of gangrene. It is, therefore, called a symbiotic or synergistic infection.

The second point is that I would like to make a plea (and I do so at every opportunity) that members of surgical departments, particularly the chairmen of those departments and the directors of surgical services, should insist upon more adequate anaerobic bacteriology in their hospitals and on their services.

FAT EMBOLISM *

ROBERT I HARRIS, F R C S (C), T S PERRETT, F R C S (C),

AND

ANGUS MACLACHLIN, M D

TORONTO, CANADA

FAT EMBOLISM occurs somewhat infrequently as a complication of fractures and of operations upon bone. Its recognition is not easy, and almost certainly, in many cases, even though they end fatally, are not recognized in their true nature. There are two reasons for this difficulty. First, in fatal cases which come to postmortem, the presence of fat emboli will not be detected unless the sections are prepared by special methods. Preparation of paraffin sections for hematoxylin and eosin stains involves dehydration in graded alcohols, and this dissolves out the fat globules. These can be demonstrated only by fat stains in frozen sections. Second, in those cases which do not end fatally, the clinical picture is not clearly defined or easily recognized. As yet, we lack a definite and certain clinical method or sign whereby the underlying pathologic cause can be recognized. At the moment, the strongest clinical evidence of the presence of fat embolism is presented by a certain rather characteristic sequence of events through which most cases pass. The sequence is as follows: (1) An injury to a bone or an operation upon a bone. (2) An interval in which the only symptoms and signs the patient presents are those related to his fractured bone, followed by (3) a period in which there develop (a) pulmonary signs and symptoms, and (b) cerebral signs and symptoms. This is followed by death or recovery. Occasionally, though rarely, fat globules may be recovered in the sputum or in the urine. These are signs of great diagnostic value but unfortunately they are rarely present, and their absence does not by any means rule out fat embolism. Similarly fat emboli in cutaneous capillaries may manifest their presence by the appearance of petechial hemorrhages in the skin. This also is a rare finding but of great value when it is present. Its absence also does not rule out the presence of fat embolism.

Because of this confusion and difficulty in clinical diagnosis, the report of a fatal case, which presented a clinical sign heretofore unrecognized, seems of value.

Case 1—Fatal case of fat embolism complicating fracture of the femur. Profound fall in hemoglobin due to hemorrhagic exudate into lungs as a reaction to pulmonary fat embolism.

S. G., male, age 22, was admitted to the hospital, July 4, 1936, with a transverse fracture of the left femur, sustained when he was knocked down by a motor car. He was conscious and not in shock. The only injury he had sustained was the fracture of the femur. Roentgenograms showed it to be a transverse fracture of the middle third of the

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939.

left femur with overlapping of the fragments and three-quarters of an inch of shortening
Temperature 98.6° F, pulse 108

Ten hours later, a Kirschner wire was passed through the lower fragment and traction applied. During the day his temperature rose to 101° F and his pulse to 120, but he was comfortable and made no complaints

Name Sam Grant

Admitted _____

Service _____

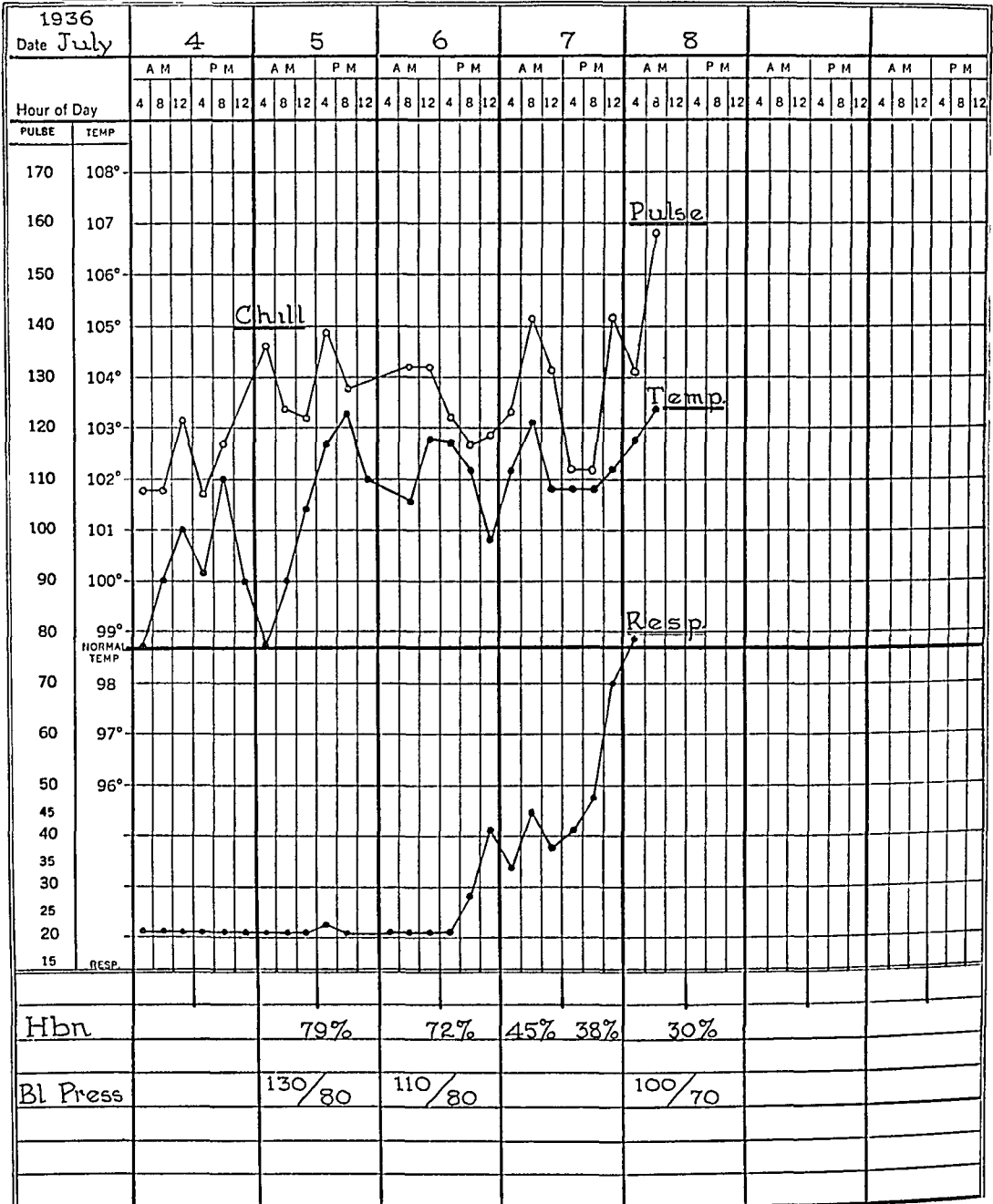


CHART I — The clinical chart of Case 1, pulse, temperature and respirations with records of the hemoglobin estimation and blood pressure

On July 5, he had a chill, after which his temperature rose to 103° F and his pulse to 140. Examination showed him to be very restless, sweating and pale. So marked was the pallor that a serious internal hemorrhage was suspected. However, no evidence of this was found on examination, nor was there a large hematoma at the site of fracture

The hemoglobin was 79 per cent. Chest examination showed impairment of air entry at the right base and a few râles. Blood pressure 130/80.

On July 6, two days after admission, a radical change had occurred. The patient was very ill, pale and irrational, pulse 130, temperature 102° F, respiration 30, hemoglobin 72 per cent, R B C 4,000,000. Complete examination revealed no findings which seemed adequate to account for this profound change. The chest findings were as previ-

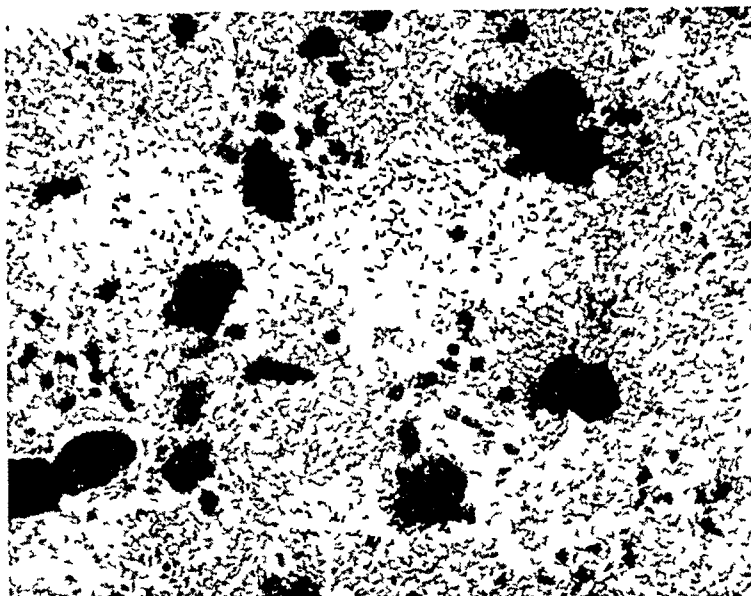


FIG 1—Case 1. Photomicrograph of the lung, showing extensive fat embolism and the alveoli filled with hemorrhagic exudate. Stained with scharlach R ($\times 160$).

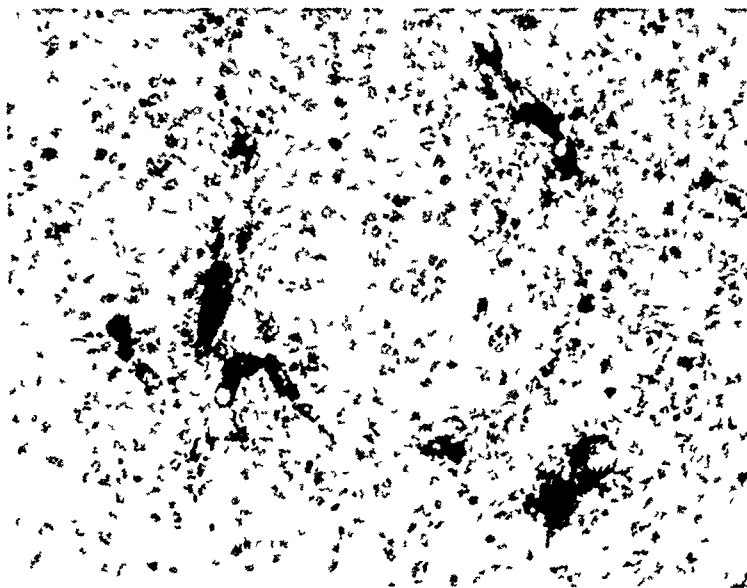


FIG 2—Case 1. Photomicrograph of the brain showing numerous fat emboli in the cerebral capillaries. Stained with scharlach R ($\times 160$).

ously noted but slightly more marked. Roentgenograms of the chest excluded the presence of blood or other fluid in the pleural cavity. During the day he became increasingly dyspneic and the respiratory rate reached 40. He presented the appearance of shock or hemorrhage and gradually became stuporous and irrational. Reestimation of the hemoglobin showed it to be 72 per cent. The blood pressure was well maintained at 110/80, in spite of the appearance of shock.

On July 7, the clinical picture was similar but accentuated, pulse 140, temperature 103° F, respiration 50. He was pale, irrational and stuporous and at times violently restless. Chest examination revealed, for the first time, consolidation involving the right lung and beginning in the left lung. Hemoglobin had dropped to 45 per cent and in the evening was 38 per cent. For the first time, cough was present and once he brought up blood-tinged sputum. Unfortunately this sputum, the only sample he coughed up during his illness, through a misunderstanding was not examined for fat. The urine contained albumen but did not contain fat droplets. There were no petechial hemorrhages in the skin.

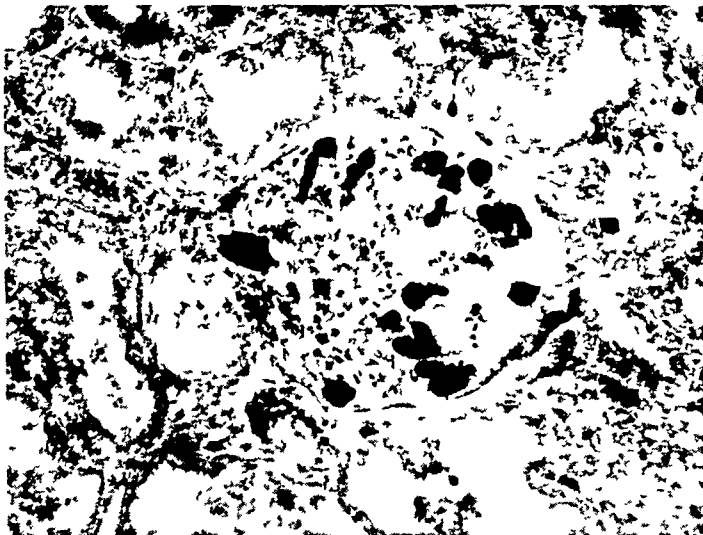


FIG 3—Case 1. Photomicrograph of kidney showing fat emboli in a glomerulus. Stained with scharlach R (×160).

The patient died the following noon, four and one-half days after his injury. Before death the pulse was 140, temperature 103° F, respiration 70, and hemoglobin 30 per cent. Blood pressure 100/70 (Chart 1). Signs of consolidation were present over the whole of the right lung and all but the apex of the left lung. On these findings a diagnosis of death from pneumonia complicating fracture was made by our medical colleagues, though past experience with fat embolism made us suspect this as the cause of death.

Pathologic Examination—Gross Lungs—Both pleural cavities were free of fluid and adhesions. Both lungs were solid and did not crepitate except for a small area in the apex of the left lung. The consolidated lungs were dark red in color, resembling liver in appearance. (Note that this could well be regarded as the picture of pneumonia in the stage of red hepatization.) Large quantities of bloody fluid could be expressed from the cut surfaces. The pulmonary vessels were free from thrombus.

Brain—The cut surface showed numerous scattered small areas of petechial hemorrhage.

Left Femur—Showed a transverse fracture with a hematoma of moderate size.

The microscopic findings were of the greatest interest and importance.

Microscopic Lungs (Fig 1)—The alveoli were completely filled with a hemorrhagic exudate consisting almost entirely of red blood cells and fluid. Unlike the picture of pneumonia, leukocytes were few in number. Stained with scharlach R, the lung capillaries were found to contain numerous globules of fat of all sizes. The picture was that of an intense hemorrhagic exudate filling the alveoli, with numerous fat emboli in the capillaries. Inflammatory cells were very few in number.

Brain (Fig 2)—Stained with scharlach R, many capillaries were seen filled with fat globules, each surrounded by a zone of necrosis.

Kidney (Fig 3) —Fat stains showed numerous globules of fat in the capillaries of the glomeruli

Liver —A few fat emboli were found here also

SUMMARY AND COMMENT —The significant findings in this case of fatal fat embolism were as follows. The course of events, broadly considered, was that of most cases of fatal fat embolism, namely, (1) a serious injury to a bone followed by (2) an interval in which the only signs and symptoms were those related to the injured bone. Then came (3) the onset of serious pulmonary and cerebral signs and symptoms, progressing to death. It is noteworthy that from clinical signs and gross postmortem evidence the pulmonary lesion might well have been regarded as pneumonia. Only the sections stained with schi-
lach R revealed the true pathology to be pulmonary fat embolism with hem-
orrhagic exudate into the alveoli.

The unusual feature of this case, or at any rate the feature which heretofore has not been recognized as an accompaniment of fat embolism, was the profound fall in the red blood cell count and hemoglobin content of the blood. So great, and so evident, was this anemia that a concealed hemorrhage was suspected. The great fall in the red blood cell count of the blood is adequately explained by the postmortem findings in the lungs. The pulmonary consolidation was due to an exudate into the alveoli which consisted almost exclusively of erythrocytes and serum. The enormous amount of this exudate would adequately account for the great and sudden fall in erythrocytes and hemoglobin in the circulating blood. We shall attempt to discuss the mechanism of its production later.

For some time prior to the occurrence of this fatal case of fat embolism, our attention had been drawn to the severe and progressive fall in erythrocyte count and hemoglobin percentage which occurred in certain patients following bone operations, notably spinal fusion and arthrodesis of the hip. It did not seem that this could be accounted for by loss of blood at the time of operation, first, because it was much greater than the blood loss and, second, because it was progressive over a relatively long period of time. Table I

TABLE I
ILLUSTRATING THE PROGRESSIVE AND MARKED FALL IN ERYTHROCYTES
AND HEMOGLOBIN FOLLOWING OPERATIONS UPON BONE UNEXPLAINED
BY PRIMARY BLOOD LOSS

Case		Hemoglobin	Red Blood Count
J D	October 11, 1933	98%	4,750,000
	October 12, 1933	Arthrodesis of Hip	
	October 19, 1933	60%	3,000,000
	October 31, 1933	45%	2,750,000
	November 28, 1933	83%	4,750,000
J B	July 23, 1935	110%	5,400,000
	August 8, 1935	Spinal Bone Graft	
	August 10, 1935	85%	4,328,000
	August 23, 1935	74%	3,616,000
	September 5, 1935	95%	4,800,000

illustrates two such examples. It is just possible that the progressive loss of red blood cells in these cases can be accounted for by pulmonary fat embolism and the accompanying hemorrhagic exudate. At any rate, the following case seems, clearly, to be a case of pulmonary fat embolism following operation, analogous to the fatal case just described.

Case 2—*Probable pulmonary fat embolism following spinal fusion for scoliosis, marked pulmonary signs and symptoms, marked cerebral symptoms and profound fall in hemoglobin. Recovery.*

A. E. R., female, age 20, was operated upon, October 22, 1936. A spinal fusion for scoliosis was performed, extending from the fifth to the twelfth dorsal spine, inclusive. Large grafts taken from the tibia were employed for this purpose. The operation was expeditiously performed and she suffered no shock. A transfusion of 500 cc. of blood was administered. For two days following operation she vomited repeatedly but otherwise seemed in satisfactory condition. On the fourth day, there suddenly developed some type of pulmonary catastrophe, characterized by cyanosis, fever (101° F.), rapid pulse (130), and increased respirations. Adequate examination of the chest was impossible because she was encased in plaster. On the fifth day, she seemed moribund. On the sixth day, delirium developed and continued for three days, notwithstanding the fact that the respiratory symptoms were improving. From the tenth day on she made steady and rapid improvement and ultimately made a complete recovery.

The acute and serious complication she passed through was accompanied by a profound fall in hemoglobin. The first record we have was 45 per cent, taken on the day of the onset of the pulmonary symptoms, and this in spite of the transfusion which had been administered following operation. Two days later it was 40 per cent, the next day 34 per cent, and following a transfusion rose to 45 per cent. On the succeeding days the estimations were 50, 62, 70 and, finally, on November 10, 81 per cent following another transfusion.

COMMENT—This, then, is a patient who, following an extensive operation upon bone, developed a serious complication manifested by cyanosis, respiratory distress, fever, tachycardia, increased respiratory rate, delirium, semi-coma and, finally, a rapid and extreme fall in hemoglobin content. The similarity to the preceding case of proven fat embolism, which was fatal, is so great that one must consider fat embolism as a probable cause of her symptoms also.

Incidence of Fat Embolism—The occurrence of fat embolism is rare but there is reason to think that it is more common than is supposed. The difficulty of recognizing the condition, both clinically and at postmortem, undoubtedly results in many cases being overlooked. Our interest in this condition was stimulated, four years ago, as the result of a postoperative death from fat embolism, proven at postmortem. The operation was an arthrodesis of a tuberculous hip. Prior to that date the diagnosis of fat embolism does not occur in the records of the Toronto General Hospital. Since then we have been able to recognize six fatal cases and in addition six nonfatal cases in which the diagnosis of fat embolism is almost certain, though without the confirmation of sections, some doubt must always exist as to the accuracy of this diagnosis. It would seem that fat embolism, even though rare, is more common than is supposed, that it is easily overlooked, and that a consciousness of its possible existence may lead to its more frequent recognition.

BRIEF CLINICAL RECORDS OF FATAL CASES OF FAT EMBOLISM

Case 1—Reported herewith

Case 2—This case has been reported previously² (J A M A., 195, 1013, September 28, 1935) A boy, age 17, suffering from tuberculosis of the hip, was operated upon for the purpose of fusing his diseased hip Transfusion of 500 cc of blood followed his operation, which presented no difficulties Six hours after operation he became cyanosed and dyspneic, and complained of a sense of constriction about the chest Cyanosis increased, pulse became rapid and feeble, and temperature rose to 103° F He died 20 hours after operation Postmortem examination revealed extensive fat embolism of lung

Case 3—A man, age 39, sustained a fractured femur in a motor accident This limb had previously been injured at the knee in such a manner as to necessitate the use of a plaster encasement for a prolonged period of time It is possible that the bone atrophy from disuse may have been a factor which facilitated the production of fat embolism Six hours after his accident he became unconscious and died 54 hours later without regaining consciousness Postmortem revealed extensive fat embolism of lungs and brain (Courtesy of Dr J L McDonald)

Case 4—A woman, age 73, sustained a fracture of the neck of the femur, May 12, 1934 It was reduced and fixed with a Smith-Petersen nail, May 17, 1934 For a few days following operation, she presented no untoward symptoms except a continuous fever She then developed respiratory symptoms and signs, followed by delirium and coma Death occurred ten days after operation Postmortem examination revealed consolidation of the lung bases and, on section, fat emboli in the pulmonary capillaries The brain was not examined

Case 5—A man, age 50, sustained a fracture of the tibia and fibula, November 28, 1935 It was reduced under local anesthesia on the day of admission On the second day he was stuporous and hard to rouse There was no evidence of head injury and neurologic examination was negative Coma deepened and râles and bronchial breathing were found in both lungs No fat was found in urine or sputum He died in coma six days after the accident Postmortem showed consolidation of both lung bases and numerous petechial hemorrhages in brain Fat embolism was demonstrated on section of lungs and brain

Case 6—A woman, age 32, was operated upon, February 17, 1937, for stabilization of the hip The operation was extensive but no great difficulty was encountered Postoperative course was complicated primarily by distention and vomiting On the second postoperative day she became cyanosed and dyspneic The distention was controlled on the third postoperative day but the cyanosis and respiratory distress increased Coma developed toward the end of this day and rapidly deepened until death One hemoglobin estimation, made on the day of her death, was 47 per cent Postmortem was not permitted In the absence of definite postmortem evidence the diagnosis of fat embolism is, of course, presumptive, but from the course it seems reasonably certain that this was the cause of death

NONFATAL CASES

Probable Diagnosis, Fat Embolism

Case 1—Reported herewith

Case 2—This case has been reported previously² (J A M A., 195, 1013, September 28 1935) A man, age 35, sustained a fracture of the tibia, April 2, 1935 The fracture was reduced, April 2, 1935 He remained conscious and mentally clear until April 5 On April 6 he became restless and uncooperative He was dull and semicomatose Temperature 102° F, pulse 180 Coughed up bloody sputum He remained comatose and irrational until April 12, when he began to improve By April 19, he had completely recovered from the cerebral lesion Urine collected, April 7, contained fat On April 16, he developed a patch of pleurisy on the right side which cleared up within two days and,

on April 23, a similar transient pleurisy occurred on the left side. The sputum was not examined for fat (Courtesy of Dr K G McKenzie)

Case 3—A man, age 31, sustained a fracture of the femur, August 17, 1938. Twenty-four hours later he became drowsy and stupefied and slowly became unconscious. Examination showed no sign of injury to head, cranial nerves normal. No paralysis of legs. There were numerous petechial hemorrhages in skin of trunk and neck. Lumbar puncture showed a pressure of 250 Mm without increased protein or cells. Bur holes in either temporal fossa showed absence of hemorrhage and the presence of a large collection of spinal fluid under tension in the subarachnoid space. Recovery followed (Courtesy of Dr E H Botterell)

Case 4—A man, age 30, sustained a fracture of the tibia. Thirty-six hours after his injury he became restless and irrational. Respirations were increased and he was cyanosed. Unconsciousness developed. The lung bases showed dulness and râles. Sputum and urine contained fat globules. After a stormy convalescence, during which there were extensive signs in both lungs, he recovered completely (Courtesy of Dr Wm S Keith)

Case 5—A man, age 19, sustained a fracture of the femur, August 6, 1938. He presented no symptoms other than those associated with his fractured femur until August 12, on which day the fracture was manipulated in an effort to secure reduction. He collapsed on the table, pulse became rapid and feeble and the blood pressure fell. This was followed by pulmonary signs and mental confusion, persisting for about two days. Hemoglobin estimation at that time was 50 per cent. He ultimately made a complete recovery (Courtesy of Dr S Gordon)

Case 6—A man, age 35, sustained fractures of the forearm and leg and was admitted in shock, October 21, 1935. Was rational on October 22. On October 23, he became comatose with stertorous breathing of intermittent rhythm. He slowly became cyanosed and dyspneic and deeply unconscious. On October 25 he had improved, though expectorating bloody mucus, and from then on he slowly recovered. He had no head injury (Courtesy of Dr Gordon Cock)

Experimental Data—The fatal case we have recorded presents two problems which demand explanation. (1) How could a relatively small amount of fat cause such a severe reaction with a fatal ending? The injury to the femur was not extensive and the resulting hematoma was only of moderate size. The amount of fat available from this fracture could not have been more than a small fraction of the total amount in the medullary space of the femur and this of itself is not very great in amount. (2) How could such a bland body constituent as fat cause such an intense irritative reaction of a hemorrhagic nature? We have attempted to find an answer to these problems by the experimental investigation recorded below. Though we have not succeeded in reproducing the profound fall in hemoglobin, we have succeeded in reproducing the lung changes including the hemorrhagic exudate.

Protocols of Experiments Using Neutral Human Fat—Rabbits of approximately the same size (2 Kg) were used throughout these experiments. Human fat obtained at operations in which bone grafts were removed from the tibia was the material utilized to cause the fat embolism. Most workers in experimental fat embolism have used vegetable or mineral oils. It seems quite possible that this does not reproduce exactly the conditions which exist in human cases. For that reason human fat was used. It is easily obtained in amounts from 10 to 20 cc from the medullary cavity of the tibia when a graft has been removed. As it is quite fluid, it can be aspirated from the bed

of the graft with a syringe. The fat was separated from the small amount of blood present by incubating the material at body temperature and subsequently decanting the clear supernatant fat.

Using such material we were able to establish that the minimum lethal dose for rabbits is 0.9 cc. of neutral human fat per kilo of body weight given in one dose. Attempts were then made to cause a fall in hemoglobin by repeated sublethal doses administered over a period of time. Repeated injections of neutral human fat in doses up to 0.5 cc. per kilo reaching in some cases a total of 15 cc. of fat per animal (approximately 7.5 cc. per kilo) could be given without causing death, though marked pulmonary symptoms (dyspnea) and cerebral signs (ataxia and incoordination) were produced. Note that the minimum lethal dose for a single administration is small—

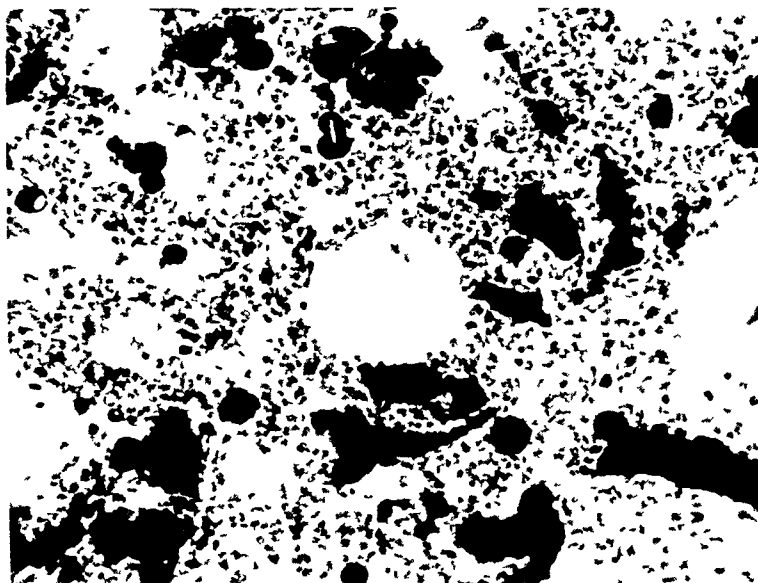
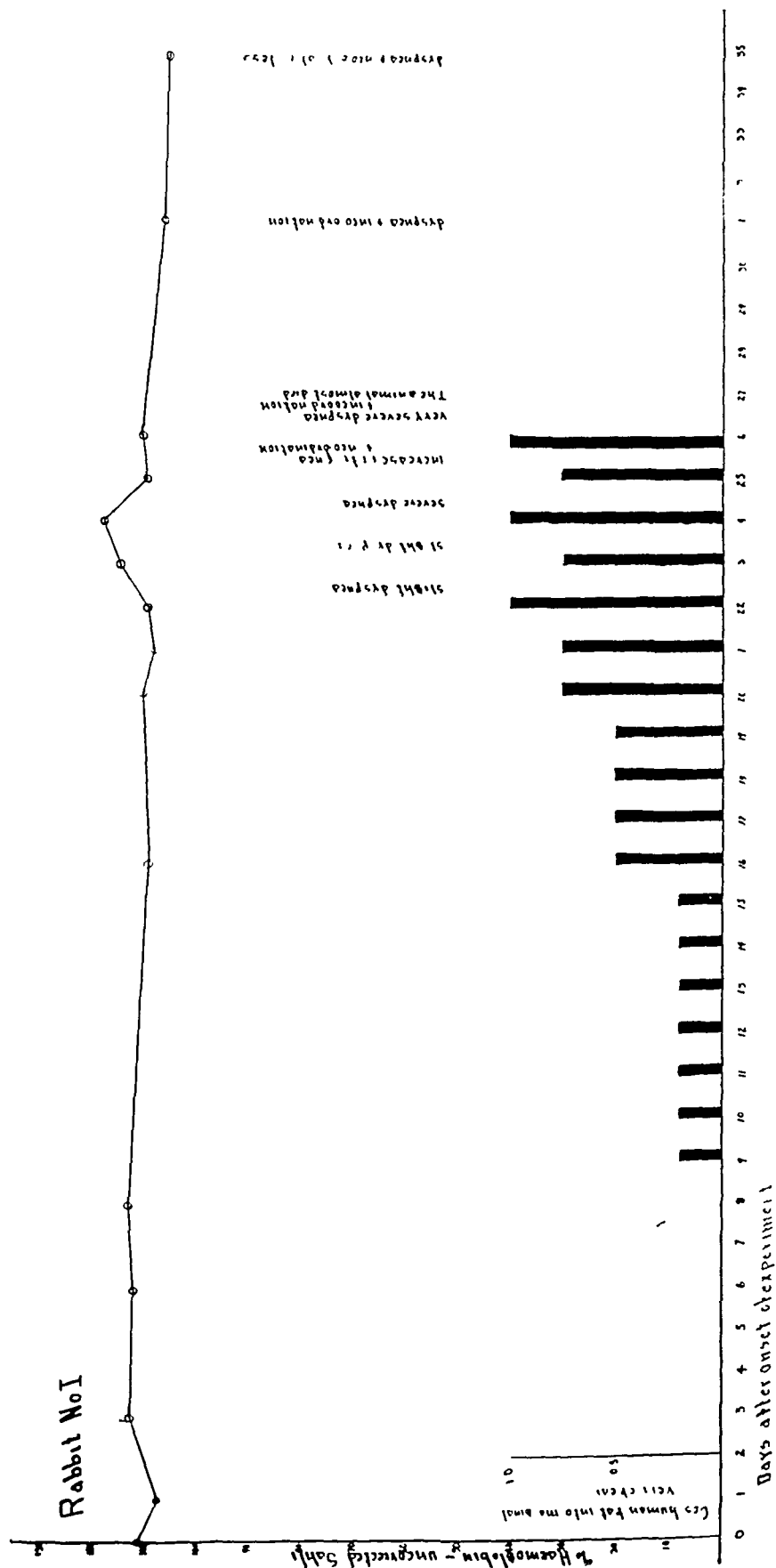


FIG. 4.—Photomicrograph of lung of rabbit following repeated injection of sublethal doses of neutral human fat. Very numerous fat emboli. Frozen section, scharlach R ($\times 160$)

0.9 cc. per kilo. This would be the equivalent of 63 cc. for a 70 kilo (150 pound) man. Note also that when half the minimum lethal dose is given repeatedly, relatively enormous amounts of fat can be administered. At post-mortem these animals showed stiff, solid lungs which looked and felt like liver, with numerous fat emboli in lungs, liver, kidney and brain (Fig. 4). The pulmonary alveoli were filled with a hemorrhagic exudate of moderate intensity. There was no significant fall in hemoglobin (Chart 2).

Protocols of Experiments Using Hydrolyzed Human Fat—The intensity and the hemorrhagic nature of the reaction in the lung and also in the brain and the skin suggest that some change may have occurred in the fat which renders it an irritating rather than a bland body fluid such as one might naturally consider it to be. We are indebted to Professor W. K. Franks, of the Department of Banting Medical Research, for the suggestion that perhaps these intensely irritating qualities are the result of splitting of the neutral fats into glycerol and fatty acids by tissue lipases, either at the site of the injury to the bone or in the lung. With this in mind another set of experiments was



FAT EMBOLISM

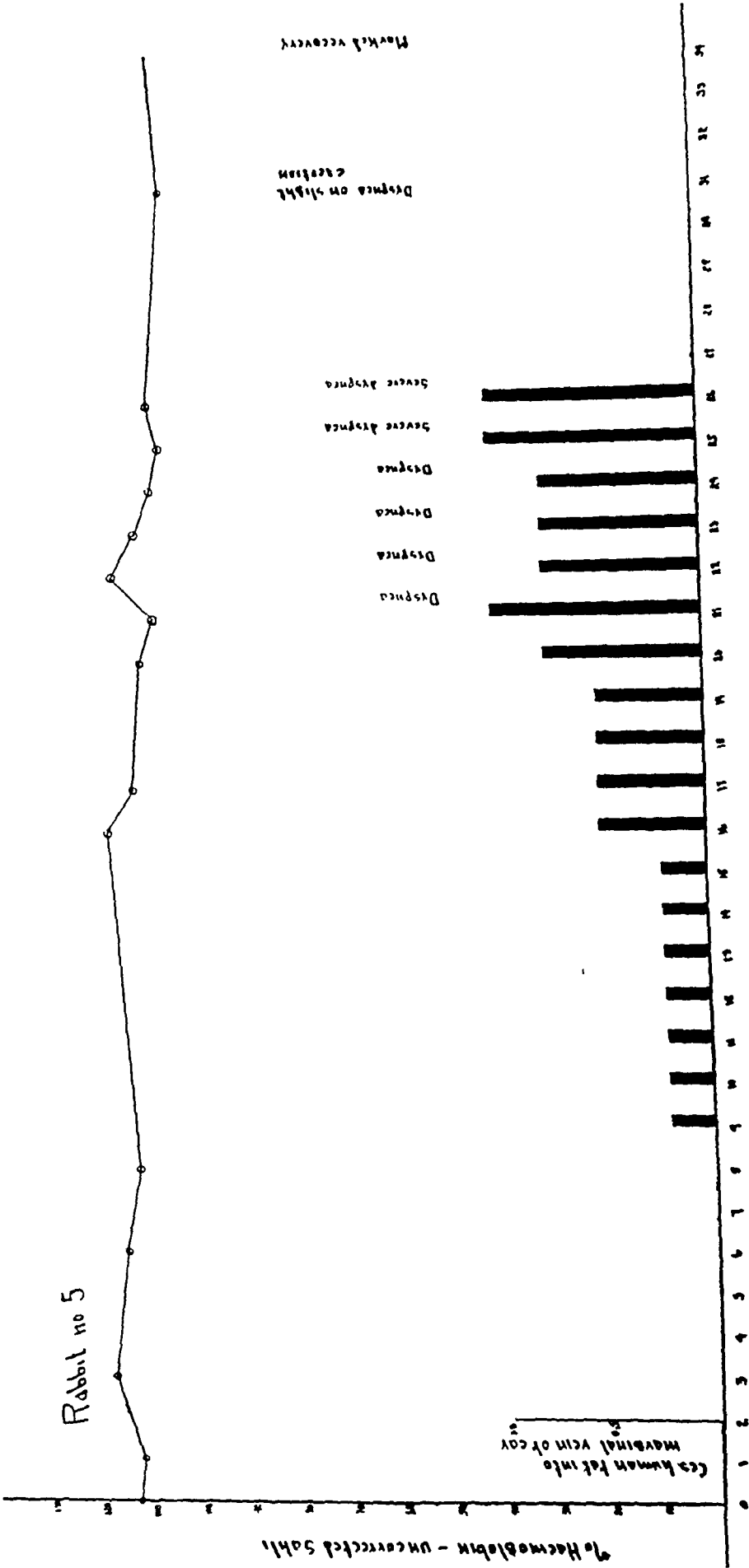


Chart 2 —Graphs of two experiments on the production of fat embolism in rabbits following repeated sublethal doses of neutral human fat

undertaken, also upon rabbits, in which human fat hydrolyzed with dilute hydrochloric acid was used. The excess of acid was neutralized by an alkali before injection.

These experiments showed that the minimum lethal dose of hydrolyzed

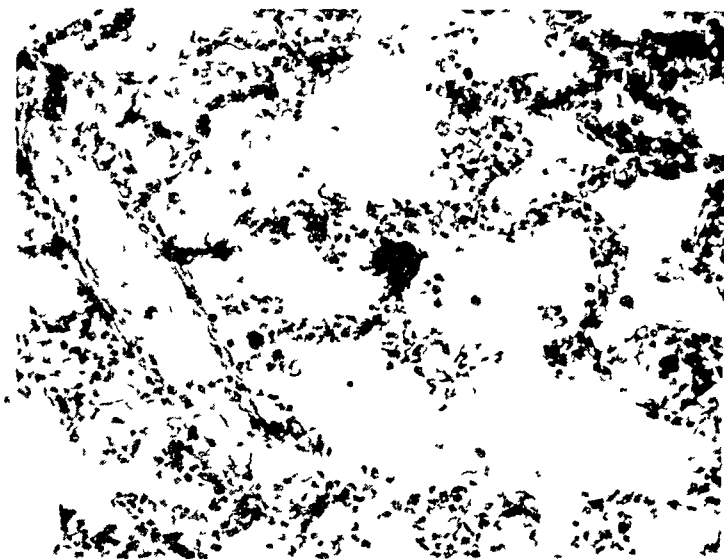


FIG 5—Photomicrograph of lung of rabbit following repeated injection of sublethal doses of hydrolyzed human fat. Few and small fat emboli. Frozen section, schirrich R ($\times 150$)

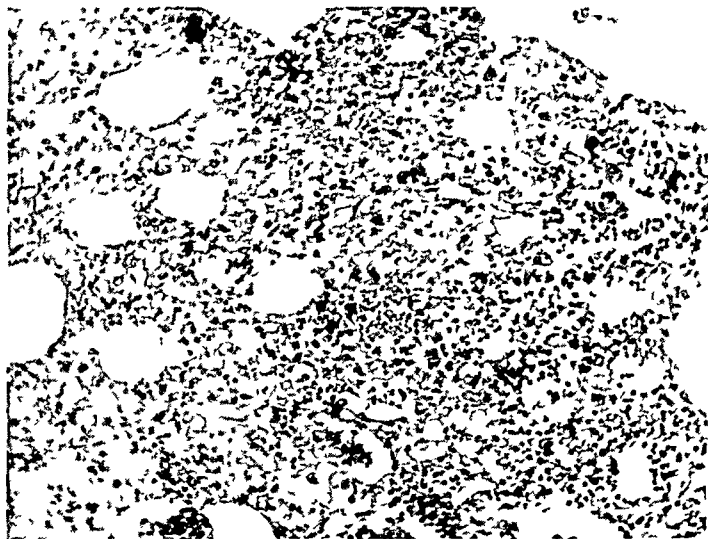


FIG 6—Photomicrograph of same rabbit's lung as Figure 5 illustrating the hemorrhagic and serous exudate in the pulmonary alveoli similar to that seen in the fatal human case. H and E stain ($\times 150$)

fat was 0.07 cc per kilo of body weight, i.e., less than one-twelfth the minimum lethal dose of the neutral fat. Repeated injections with 0.035 cc per kilo (one-half the minimum lethal dose) were all fatal in five doses. The hydrolyzed fat, therefore, is very much more toxic in single doses than neutral fat, and repeated injections of small doses are tolerated much less well. Postmortem examination showed only a few fat emboli in the lungs

but the alveoli were filled with a hemorrhagic exudate closely resembling that seen in the fatal human case recorded (Figs 5 and 6) No significant change in hemoglobin content of the blood was observed (Chart 3)

COMMENT—These experiments demonstrate certain facts of importance. The administration of a comparatively small amount of fat in the single dose is rapidly fatal. If the fat is administered in small repeated doses over a

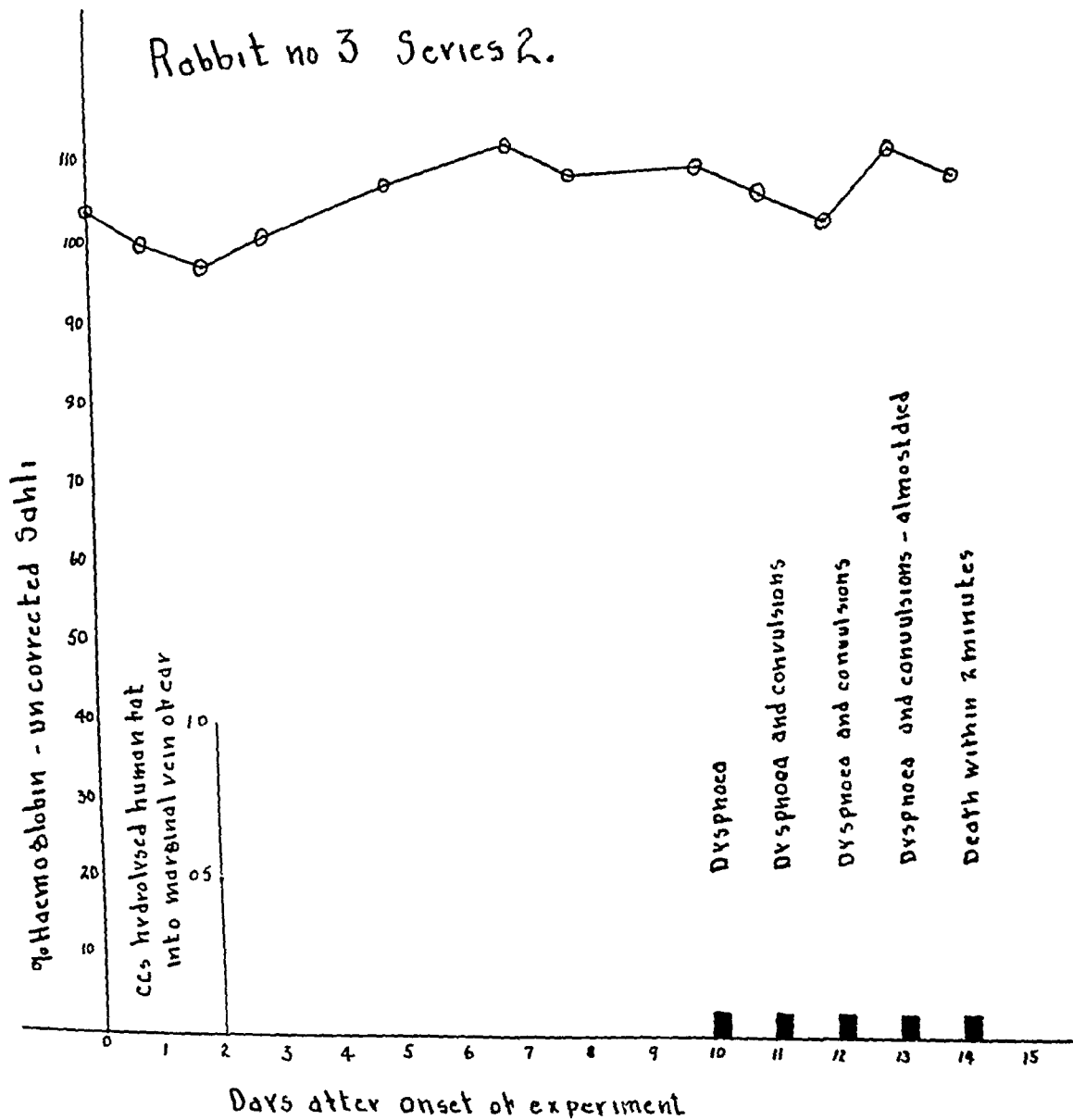


CHART 3—Graph of an experiment on the production of fat embolism in a rabbit following the repeated injection of sublethal doses of hydrolyzed human fat

period of time, a comparatively large amount of fat can be given. The changes produced are similar to those seen in human cases, namely, consolidation of the lung as the result of a hemorrhagic exudate into the alveoli and numerous fat emboli in lungs, brain and kidneys. The clinical symptoms which accompany these changes are predominately respiratory and cerebral. Though we did not succeed in reproducing the fall in hemoglobin, it was possible to duplicate the hemorrhagic exudate in the lung. Of the greatest significance was the demonstration of the fact that hydrolyzed fat is much more toxic than neutral fat and produced a far more intense hemorrhagic

exudate It strongly suggests that the serious effect of fat embolism results in part from an alteration in the fat which renders it more irritating and that this change is of the nature of hydrolysis by lipases and that the fatty acid or resulting soaps are the irritative substances

Mechanism Whereby Fat Embolism Develops—Fat embolism occurs when free, fluid fat enters the vascular system and is carried by it to a capillary bed There the globules of fat are sufficiently large to occlude the lumina of a greater or lesser number of the capillaries Only under certain special circumstances can fat embolism occur It is necessary first of all that fat be freed from fat cells This implies some kind of trauma which will rupture the envelopes of the fat cells Second, the fat must enter the venous circulation As veins commonly collapse when they are opened, fat embolism will occur only under circumstances in which the sectioned veins remain open But open veins bleed, and this implies a flow out of the vein rather than into it Fat can enter veins only if it accumulates at a pressure greater than venous pressure and so is forced into the open vein Three things, therefore, are necessary before fat embolism can occur (1) An accumulation of fluid fat freed from its cellular envelope by trauma (2) Open veins, the open ends of which do not collapse (3) The accumulation of the fat under a pressure greater than venous pressure so that it can be forced into the open ends of the veins

Though fat must be freed from its cellular envelope and veins cut across in many operations, and often by trauma, only under special circumstances do the veins remain open and the fat accumulate under a pressure sufficiently great to force its way into the veins Injuries to bone provide exactly the factors necessary for the production of fat embolism There is abundance of fat in the bone marrow easily set free by the trauma of fracture or operation The veins are held open by their attachment to the bony haversian canals in which they run It is not difficult for the wound exudate to accumulate under tension In operations upon soft tissues, the reverse is the case Though there is abundance of adipose tissue and though much fat may be freed, entrance into the veins is prevented by collapse of the veins and the diminished likelihood that the wound exudate will accumulate under tension Exudate from soft tissue wounds seeps out along the line of suture There is less opportunity for the application of firm dressings and hence less sealing of the exudate within the wound Hence, fractures and operations upon bone constitute the most frequent antecedents of fat embolism

Pathology of Fat Embolism—Once fat has been forced into the venous system, it is carried by the circulation to the pulmonary capillaries There a varying amount of occlusion occurs dependent upon the size of the globules, the total amount of fat which enters the circulation and the rate at which it reaches the lung A small quantity of embolic fat will create less disturbance than a large quantity, and the same quantity introduced rapidly will produce severe or even fatal results, while introduced over a long period of time or in repeated small doses, it will cause little harm In the lung the presence

of fat emboli occluding the pulmonary capillaries (1) interferes with normal oxygen exchange, (2) obstructs the pulmonary flow and hence causes dilatation of the right side of the heart, (3) causes an exudate into the alveoli. It has been noted by Grosskloss¹ and others that this exudate consists largely of erythrocytes and serum, but the accompanying fall in hemoglobin has not been recorded before.

The flood of embolic fat may be sufficiently great to cause death from pulmonary embolism in a short time. This accounts for certain deaths on the operating table or shortly after operation. In less severe cases, some of the pulmonary emboli are forced through the lungs and reach the systemic circulation through the left side of the heart. The fat again comes to rest in the systemic capillaries. The resultant symptoms are dependent upon the nature and importance of the organ whose capillaries are involved. Cerebral embolism is the most common, most important and most serious manifestation. In the brain, capillaries are occluded by the fat droplets, a narrow zone of brain tissue undergoes necrosis and the area of necrosis is surrounded by a zone of hemorrhage. This, in the gross, gives rise to the characteristic "ring hemorrhages." It is worthy of note that in the brain, as in the lung, the reaction induced by the fat emboli is hemorrhagic.

Though the cerebral lesions are the most important of the peripheral manifestations, emboli may occur in any organ. Two other sites of importance are the kidney and the skin, chiefly because they provide us with a means of diagnosis. Of the fat emboli which reach the kidney, a certain number rupture the glomerular capillaries and reach the urine where they can be recognized by appropriate measures. In the skin fat embolism produces a hemorrhagic reaction similar to that produced in the brain. The importance of these petechial skin hemorrhages lies in the strong confirmation they give to the diagnosis of fat embolism when the clinical syndrome suggests this complication.

SUMMARY—The object in presenting a fatal case of fat embolism is to call attention to the existence of this complication of fractures and operations upon bones. Though of infrequent occurrence, it is of serious importance because of its high mortality. It is not easy to recognize either clinically or at postmortem for reasons which have been stated. The most valuable means of recognition still is the rather characteristic sequence of events in the clinical course: (1) An injury to a bone, (2) an interval in which the only symptoms are those related to the injured bone, (3) the development of pulmonary signs and symptoms, and (4) the development of cerebral signs and symptoms. Fat globules in the sputum and in the urine are of great diagnostic value in those cases in which they appear. Petechial hemorrhages in the skin are also of great diagnostic value when they occur.

To the somewhat meager group of signs and symptoms which are of diagnostic value we have added one further sign, namely, a profound fall in hemoglobin in an illness which complicates a fracture and follows the course outlined above. This sign is the result of the loss from the circulation of

great numbers of erythrocytes which are poured into the pulmonary alveoli in the hemorrhagic exudate which is called forth by the presence of fat emboli in the lung. It is worthy of note that in lung, brain and skin the characteristic response to fat embolism is a hemorrhagic exudate. The fall in hemoglobin noted in the two cases presented in this paper will occur only in those patients who have an extensive pulmonary exudate. Hence, we cannot expect to find it in every case of fat embolism. But when it does occur, and in company with the train of clinical events mentioned earlier, it is, like fat in sputum and urine and like petechial hemorrhages in the skin, strong confirmatory evidence of fat embolism. Those cases which are rapidly fatal from massive pulmonary fat embolism will not display it because there will not have been sufficient time to develop the hemorrhagic exudate. Similarly, the mild cases will not display it because the extent of the exudate is small. It will occur only in patients who sustain an extensive but not rapidly fatal fat embolism of the lung and who survive for a length of time sufficient for the development of extensive alveolar exudate. In such cases, however, it may be a valuable confirmatory sign of the disease.

The experiments we have conducted strongly suggest that the intensely irritating effect of fat embolism is the result of a change in the fat and that this change consists in the splitting of the fats by tissue lipases so as to free the irritating fatty acids. It will be necessary to develop these experiments further before definite conclusions can be reached.

CONCLUSIONS

(1) Fat embolism, though uncommon, is a more frequent complication of fracture and of operations on bone than is commonly supposed. An appreciation of its existence will lead to its more frequent recognition.

(2) It is difficult to recognize clinically because of the lack of specific and constant signs, and pathologically, because of the necessity of unusual staining methods.

(3) Points of value for diagnosis are (a) The rather characteristic sequence of clinical events, (b) the occasional presence of fat in urine, fat in sputum and petechial hemorrhages in the skin. To this we would add, in certain cases, a profound fall in hemoglobin.

(4) The serious pathologic changes produced by fat emboli are probably due in part to the freeing of fatty acids by the action of tissue lipase.

REFERENCES

- ¹ Grosskloss, H. H. Fat Embolism. *Yale Jour. Biol. and Med.*, October-December, 1935, January, 1936.
- ² Harris, R. I. Fat Embolism. *J. A. M. A.*, 1935, 1013, September 28, 1935.

DISCUSSION—DR. J. DEWEY BISGARD (Omaha, Neb.) This has been a most interesting presentation of a subject which I believe has received too little attention. My experience has been similar to that of Doctor Harris, that is, after becoming interested in the subject, I have seen much more clinical evidence of it.

Since the few cases of fat embolism which I have observed occurred in patients which had had either no anesthetics or anesthetics which contained no ether, and since ether is a fat solvent, the question of possible protection by ether against fat embolism was raised. Bone marrow fat from both tibiae of rabbits was macerated in a mortar and suspended in salt solution. This suspension was injected into the veins of the ears of other rabbits, in one group, during deep ether anesthesia, and in the other group of unanesthetized animals, which were used as controls. The lungs were examined for fat by Doctor Baker, a pathologist, and graded quantitatively by him with variations ranging from a trace up to four.

In the first group of animals there was a five-minute interval between injections and recovery of specimens. One cubic centimeter was injected, and the controls showed very much more fat than did the ones that received the injections while deeply anesthetized. Thirty minutes after injection of one cubic centimeter, there was still a striking difference between the controls and the etherized animals. Forty-eight hours later, however, the etherized group contained more fat than did the controls, and at 14 days, distinctly more.

Now, the question came up whether this fat passed on through into the peripheral circulation as a result of dilatation of the capillaries accompanying etherization, or whether the ether had some solvent action upon the fat. In answer to this question, we sectioned other tissues, liver, spleen, lung, brain, and heart, and in no instance did we find any fat emboli. Thus we concluded that the ether broke down the fat which circulated unobstructed until the ether was eliminated. As ether was given off in the lungs, the fat reappeared in the pulmonary capillaries in globules. When given intramuscularly, again the fat was found in the lungs, but in these instances principally in the alveoli, some in the capillaries, but in each instance in phagocytes. Apparently it was transported by these cells from the site of injection.

I made a series of experiments determining the influence of the tourniquet upon embolization of fat. Fat suspensions were injected into veins of the leg with the tourniquets applied above the sites of injection. The applications of the tourniquet for 15 minutes as compared to 45 minutes, resulted in much less fat in the 45-minute specimens. These observations were made with the veins closed and intact. Then studies were made with open veins, that is, after injection the veins were severed and the tourniquet removed either rapidly or slowly. In the latter, constriction was released to a degree that permitted arterial circulation to take place but yet maintained venous obstruction and caused considerable bleeding from the cut ends of the veins as compared to the lesser bleeding and lesser washing out of fat following the immediate release of the tourniquet. There was much less intravascular pulmonary fat in animals in which the tourniquet was released slowly.

The effect of drainage was investigated. Following wound drainage, distinctly less fat was found in the lungs than when the wounds were not drained and when the openings in the medullary canals were sealed with bone wax. In this latter group the medullary canal was opened and the fat macerated with a flexible probe.

As possible suggestions for aids to the prevention of fat embolism we might consider anesthesia as having some influence, ether a beneficial one possibly. I do not know. The use of a tourniquet during operation and slowly released afterwards minimizes the immediate influx of fat and may prevent an early postoperative catastrophe. Hemostasis is unquestionably helpful in minimizing the pressure accumulating within the medullary canal, which forces fat into the circulation, as is also drainage of the medullary canal for four days, again to relieve pressure. Gentle manipulation and rigid immobilization of

fractured and traumatized bone are recommended as time-honored, general fundamental principles

DR ARTHUR W. ELTING (Albany, N. Y.) Some ten years or more ago, I reported, before this Association, a study of fatal fat embolism to a rather incredulous audience, based on the subject matter of the paper, until we produced a series of slides which showed such a wide dissemination of fat throughout all the organs that even the most incredulous were willing to recognize that fat embolism was somewhat of an entity and might be a very serious one.

I expressed the view at that time, and I express it again to-day, based on a great deal of subsequent experience and careful observation, that fat embolism in a mild degree is of not infrequent occurrence. It does not always produce distinctive symptoms, it may not produce even suggestive symptoms, but to one who, in the language of Doctor Rodman when he spoke of being heart-minded, has occasion to treat cases of traumatism, if he is fat embolism-minded, he will be aware of more cases than if he does not think in those terms.

I may say that my original interest in this, of course, was first from a purely academic standpoint, but a case presented itself of a young man with a fractured humerus in whom, inside of 48 hours, rather serious complicating, apparent cerebral symptoms developed. I sought the assistance of Doctor Aichambault, a noted neurologist, but I told him before he saw the patient that I would make the diagnosis for him because I had never seen a case of it, and, therefore, felt that I could make such a diagnosis, namely, that it was a case of fat embolism.

He was rather skeptical about my diagnosis. However, the patient eventually came to autopsy, after running a course exactly like that illustrated by the chart of the fatal case that Doctor Harris has reported. At autopsy, numerous petechial hemorrhages were found scattered generally throughout the body. They were not noticeable on the surface of the body, however, and the pathologist drew the conclusion that we were dealing with a rapidly fulminating Streptococcic infection. I still clung to my diagnosis, and of course they saw no evidence of fat. I insisted that the tissues must all be stained for fat, and in a few days he reported to me that the smaller vessels were uniformly plugged with fat throughout the organs studied.

I felt as a basis of our study, and I feel to-day as a basis of our continued observation, that fat embolism manifests itself in different forms, in varying degrees. I have regarded the pulmonic form as perhaps the more frequent one, the cerebral form as usually or very apt to represent a final stage. I also feel that the age of the individual has a good deal to do with this.

A few years ago, one of my assistants cared for a simple fracture of a tibia in a small child, six or eight years of age. He thought it was desirable to perform an open reduction because of serious displacement and inability to reduce the fracture. In some 48 hours the child's temperature went up pretty high and it showed the evidences of what was supposed to be infection. At the same time the patient became quite disoriented and evidenced some cerebral symptoms. I was asked to see the case and looked at the wound. It seemed to look all right, and I made a diagnosis of cerebral fat embolism. The next day the child was in deep coma and apparently dying. I remember showing that case at one of my clinics as a typical case of fat embolism. I ventured the prognosis that in spite of the deep coma, because of the youth of the patient that recovery would be probable. Fortunately, I guessed right. In a few days the coma lessened very much as in the case of Doctor Harris' recovery, and the child got well.

I found from my study at that time that there was a conviction among

certain writers that in youth fat embolism is not nearly so serious a malady as in those of more advanced age. Furthermore, it seemed evident that fat embolism did not depend upon the extent or severity of the traumatism. That, it seems to me, has always been a remarkable feature. Many times since then, however, we have seen, and I am sure you have all seen, mild cerebral disturbances, a little disorientation, a little delirium, and mild, unexplainable cerebral disturbances during the days following an injury or fracture, where perhaps you have offered no particular explanation.

I found shock and infection were two of the diagnoses often made in cases I believed to have been instances of fat embolism. Furthermore, unless the surgeon has it in mind, and unless he insists that the pathologist especially examines the tissues for fat, it is not going to be recognized. We have found very serious fat embolism in cases in which we believed it played a rôle in death as well as in cases who died from other causes after severe traumatisms of bone, simply because the pathologist was made fat-minded and felt that he had to give an excuse if he did not supply us with a very good reason for not examining the tissues, especially the lungs, the brain and the kidneys for fat. It will also be found in the pancreas, the heart and all the other organs if pains are taken to look for it.

I feel it is an important matter to again have our memory refreshed. I have been wondering, during these years since I made my original report, why fat embolism received so little attention, because I cannot think that we have had anything particularly unique in our relatively limited experience in so small a community as Albany.

DR WILLIAM DARRACH (New York). During the last ten years, over 12,000 fractures have been treated on the Fracture Service of the Presbyterian Hospital. Of these, two cases have shown evidences of fat embolism. One of these is herewith reported.

Case Report—C B, female, age 72, was admitted to the hospital, November 22, 1937, having been knocked down by an automobile one hour previously, and suffered a compound fracture of both bones of the left leg, fracture of distal third left ulna, a scalp wound and cerebral concussion. She was transported by ambulance, a Thomas splint having been previously applied. On arrival, she was confused and in moderate shock. After rest, heat, two infusions of 500 cc each of Ringer's solution, a transfusion of 300 cc and 10 cc of eschatin, she was taken to the operating room and the compound wound of the leg debrided, the fracture reduced through a separate incision and a four-screw, stainless steel plate applied to the tibia. Both wounds were packed with vaseline gauze and left open. A closed reduction was carried out with the ulnar fracture. The scalp wound was debrided and closed. She was returned to bed in very good condition.

A second transfusion was given the following afternoon. For the following 24 hours the patient was restless and somewhat disoriented with some stiffness of the neck. Whether this was due to lame muscles from her injury or to subarachnoid irritation was not known. At this time, her temperature was 101° F, pulse 110, respirations 30. The second day after operation her temperature gradually rose to 102° F, pulse 120, respirations 36. There was almost no cyanosis or air hunger. On the morning of the third day she became more comatose and more cyanotic. Respirations were 26, with an increase of rigidity of her neck. Coarse, moist râles were heard at both bases. Seventy-two hours after injury, the lung sounds became much more moist with many coarse râles, cyanosis increased, her pulse remained strong and regular. Four hours later she suddenly stopped breathing. She died apparently from respiratory failure. Except for a heavy trace of albumin and a few casts the urine was normal, no fat being found.

Autopsy showed extensive fat emboli of the pulmonary capillaries with marked

stasis and a very early inflammatory reaction (Fig 1) Frozen section of the brain showed no fat emboli

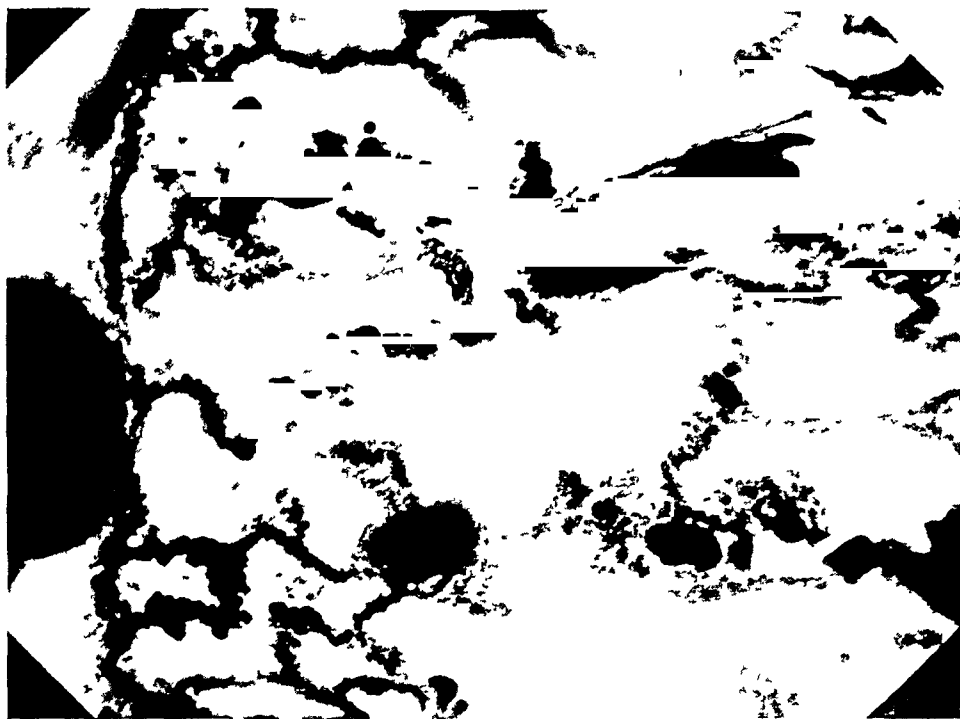


FIG 1 --Photomicrograph of lung showing extensive fat emboli in the pulmonary capillaries, marked stasis and an early inflammatory reaction

DR ROBERT I HARRIS (Toronto, Canada) I am grateful to Doctor Bisgard for bringing to my attention, and to the attention of this Association, the work he has done on fat embolism. The subject is so inherently difficult, and so obscure in its manifestations, that it is much in need of investigation which will elucidate the obscure aspects of the disease.

In my paper I deliberately avoided any discussion of treatment, wishing to concentrate upon what I felt was a new manifestation of the disease, even though it was of minor significance. My feeling is that any additional sign which might facilitate the diagnosis of fat embolism was worth reporting and recording.

If I were to say anything about treatment, it would be that measures designed to remove the hematoma and its associated fat should be the background of treatment. That is to say, drainage of areas of operation upon bone, the use of a tourniquet during operations upon bone, and aspiration of any hematoma about a fracture.

I am grateful also to Doctor Elting for his contribution to the discussion, and if I may, with his consent, carry on the torch of the fat embolists, I shall be proud to do so.

REPORT ON THE AMERICAN BOARD OF SURGERY*

EVARTS A. GRAHAM, M D

ST LOUIS, MO

THERE have been so many questions asked about the activities of the American Board of Surgery, or rather, about the progress which is being made, that the officers of the Association felt it was desirable to have a statement made at this meeting

I should like to say first of all that there were 1,570 applications received for the Founders Group of the Board. Of this number, after careful scrutiny in every way that the Board knew how to make of the fitness of these men for membership, certificates were given to 938. That is approximately 60 per cent of those who applied. I might say, however, that that is not really a fair indication because of those who merely sent in applications and who had not already demonstrated the superior training and ability in surgery by being a member of the component organizations or by holding a professorship or an associate professorship in one of the recognized medical schools, a much larger percentage than 40 per cent were rejected. I cannot give you the exact figure of that number.

There have been 423 candidates submitted to examination, excluding 86 who have just been examined in New York during the first three days of this week. Of this number there have been 205 who have finished Part II of the examination, the rest were examined only in Part I.

There were 29.3 per cent failures in the examination. Possibly some of you may think this is not a high enough mortality, others may think that perhaps the mortality is excessive. At any rate, for the benefit of those who think that perhaps the mortality is not sufficiently high, I wish to call your attention to the fact that this examination represents really the third hurdle that the men have gone over who have taken it. The first hurdle, is as careful a scrutiny as the Board can possibly make concerning the man's fitness to take the examination, that is determining his previous training, *etc*

The second hurdle, is a personal inspection of a man's performance in the operating room, carried out either by a member of the Board or by some man already certificated by the Board in whom the Board has confidence.

There have been a considerable number of rejections along the way. Therefore, when I state that there have been 30 per cent of failures in the examination, it would probably be more fair to say that 40 to 50 per cent of those men who have applied for the privilege of taking the examination have failed to make the grade.

There are certain things that have come out that are of considerable interest in these examinations, and I would like to take a minute or two to dwell upon

* Read before the American Surgical Association, Hot Springs, Va., May 11, 12, 13, 1939

at least one of these points, because it is a matter which I think concerns every one of us here who is concerned in any way with the teaching of surgery. We have found that, as a whole, the men are fairly good on their clinical surgical work. We have found that they are also fairly good in the examination which is given them in anatomy. We find that in pathology, however, they are *astoundingly* weak, to a degree which is almost unbelievable.

I should like to say something about my own experience, for instance, last Monday in this examination in New York. As part of the gross tissues which we had for examination by candidates, I had a fresh, nodular thyroid which had been removed only two or three hours before. The specimen was in excellent condition, and looked exactly like a specimen that had just been removed from the patient. There was nothing especially unusual about it. I examined nine candidates, to all nine of whom I showed this specimen, because of the remarkable display of ignorance of gross pathology which the first candidate had shown. The first candidate whom I had, told me that this specimen was probably a pancreas. I asked him if there was anything the matter with it, and he said no, he would regard it as a normal pancreas.

Incidentally, with references to what has just gone on here before, I might say that I said, "Well, then, you think this is probably an autopsy specimen?" He said, "No, I understand that Doctor Whipple is removing the pancreas! This was probably removed at operation"—but it was regarded as a normal pancreas.

The next man who saw this specimen said it was clearly a lipoma. A third man, not in succession but a little later in the series, said that he was not able to tell from what part of the intestine it had come, but obviously it was from the intestine, because it had intestinal mucous membrane on it.

I do not know what the explanation is of such appalling ignorance in gross pathology. I would have thought, before personal experience with these examinations—we have had six of them now—that such a thing would have been impossible on the part of anyone who was performing general surgery.

I might say that these three men were not men who confine their work, we will say, to fractures or orthopedic work, or something of that sort, but they were men who were trying to qualify themselves in general surgery, including thyroid work.

My experience was not unique. The experience of all the other examiners was practically the same as regards pathology, and neither was the experience in New York unique. We have met with that experience all over the country where we have given these examinations.

The importance of this observation, it seems to us who are teachers and who are conducting services for the graduate training in surgery, is that we must see to it that men who are spending a number of years in getting a graduate training in surgery, must have during their course of training sufficient experience in gross pathology to avoid such catastrophic ignorance as many of these men are presenting.

We do fail these men in their pathology when they make the deplorable

exhibits of themselves as these men have, and we compel them to take a re-examination in pathology. This has had a very wholesome effect. Some men who have failed in pathology, for instance, at a previous examination, come up again for a new examination with the statement that now they have spent a year learning pathology, and I think almost without exception they have made a very creditable performance on their second appearance.

I might say in reference to this fact, also, we have positive knowledge that in many instances courses of graduate training in surgery have been altered so as to provide for those men who are being trained in surgical careers, during their hospital work, long periods of uninterrupted time when they will get a pretty sound training in pathology, both gross and microscopic.

I look upon this observation, which I have just cited in reference to pathology, as a most astounding discovery. I would not have thought that it was possible that young surgeons who otherwise have obtained a pretty good training, could have been so deficient in one of the fundamental features of surgery, namely, pathology. I feel that the fact that the Board has made this discovery will accomplish much good, and that if it has not accomplished anything else, the fact that it has noted the woeful lack of pathologic training has perhaps more than justified its existence.

I would like to say one more thing. This is in defense of the Board. There have been many criticisms of all kinds, you could not possibly think of one that has not been leveled against the Board. The Board is glad to receive these criticisms and to do what it can to correct them. We have been in existence only a little more than two years. We realize that the whole business is somewhat experimental from the standpoint of its operation. We realize that changes will have to take place in the ultimate procedure of qualifying men for this certificate. We do, however, hope that you will realize that this is an enormous task, that all of the members of the Board spend a very great amount of time on this work. We are very glad indeed to do it. We do not mind receiving the blows and the criticisms from it, but we do hope that you will be perhaps somewhat charitable toward us for a year or two longer until we can get the whole affair working in a more efficient way.

When I state that we have been working hard, I wish to tell you that the Board meets at least twice a year, and generally three times, for periods of three or four days. The work of the Board runs continuously from nine o'clock in the morning until eleven o'clock at night, except for usually about an hour for lunch and an hour for dinner. Those of us who are ordinarily actively walking around and standing on our feet feel it a hard task to sit down for so long a period of time.

BRIEF COMMUNICATION AND CASE REPORT

FATAL PULMONARY EMBOLISM FROM SUPERFICIAL THROMBOPHLEBITIS

CASE REPORT

D WOOLFOLK BARROW, M D

LEXINGTON, K1

FROM THE DEPARTMENTS OF SURGERY, TULANE UNIVERSITY, CHARITY HOSPITAL AND LEXINGTON CLINIC,
LEXINGTON, K1

LIGATION of a superficial vein proximal to an area of superficial thrombophlebitis has been advocated by Bancroft¹ Edwards,² Eisenklam,⁴ Faxon,⁵ Freeman,⁶ Homans,⁷ O'Neil,¹⁰ Sears,¹¹ Stone,¹² and others, not only because it affords symptomatic relief, but also because it is believed it lessens the likelihood of pulmonary embolus. The following case report emphasizes the importance of such a prophylactic surgical procedure.

Case Report—F O B, white, female, age 49, was admitted to the New Orleans Charity Hospital October 14, 1938, complaining of pain in the left leg of 11 days' duration. This had begun after bruising the left calf, 11 days previously. The pain was confined to the lower leg at first, but, at the time of admission, it had extended to the groin, and was aggravated by walking. The patient said she had had five mild chills prior to entry.

Twenty-eight years previously, soon after the birth of her first child, the patient had had a sudden onset of tremendous swelling and discomfort in her left leg. A diagnosis of phlegmasia alba dolens (milk-leg) was made. Her immediate discomfort was relieved by rest in bed, but ever since that time the patient had noticed dilated, tortuous superficial veins of the left leg. Subcutaneous rupture of one of the varices resulted in localized pain and a residual hematoma which was slowly absorbed. Subsequently she had a similar episode. There had been no ulceration of the leg. Five years before entry, the patient had a cholecystectomy and incidental appendectomy performed, without post-operative complications. She had had whooping cough, chickenpox, measles, malaria, and rheumatic fever in childhood.

Physical Examination—The patient was obese, and was able but reluctant to walk because of the aggravation of pain which this caused in her left leg. The left leg showed multiple, tender, nodular, cord-like swellings along the course of both the long and short saphenous veins. The left calf was slightly larger than the right, and the subcutaneous tissues were indurated. There was no detectable difference in temperature on the two sides. The dorsalis pedis arteries on both legs were readily palpable. Blood pressure 150/90. Pulse on admission was 103 and varied from 80 to 103 during the course of her stay in the hospital. Temperature was 97.7° F on admission and varied between 97.7° and 100° F. White blood count 14,500 on admission, urine negative.

Subsequent Course—Ligation of the saphenous vein was proposed, but was not carried out, not only because it was felt that the thrombi were too widespread to be favorably affected, but also because the patient's symptoms subsided so rapidly on con-

Submitted for publication January 9, 1939

servative treatment Although the patient was anxious to go home she was kept in bed, since localized tenderness remained

On the fourteenth day at 5 30 A M the patient experienced sudden pain under the sternum immediately after exerting herself to get on the bed pan The pain was followed by profuse sweating, dyspnea, cyanosis and death in a very few minutes

Autopsy—The superficial veins of the left leg were irregularly distended and contained firm clots These did not extend into the deep venous system at any point On microscopic examination the clots were found to be partially organized

The lungs were reddish-purple in color, boggy in consistency, and weighed 1,300 Gm On section the entire parenchyma was edematous The bronchial tree and hilar lymph nodes were normal A loose fitting thrombus filled the pulmonary artery and extended into the left main branch The inferior vena cava, portal vein, iliac vein and femoral vein contained no thrombi The pathologist, on the basis of his examination, felt that the pulmonary embolus arose from the left great saphenous vein

Although such serious sequelae following superficial thrombophlebitis are not commonly found, Nobl⁹ found that 0.5 per cent of fatal pulmonary emboli arise in superficial veins Proximal ligation of such a superficial thrombophlebitic vein would not only minimize the danger of such a disastrous complication, but has, in our experience, relieved the patient's symptoms Furthermore, since destruction of venous valves seems to be an inevitable sequela to thrombophlebitis,³ the affected vein, if not already varicose, will become so, so that ligation will eventually be necessary, the technic of which should follow the accepted surgical methods of treatment for varicosities of the group of veins so affected¹¹ We have not encountered wound infection in patients thus treated nor has it been reported in the literature

REFERENCES

- ¹ Bancroft, F W Proximal Ligation and Excision of Veins for Septic Phlebitis *ANNALS OF SURGERY*, 106, 308, 1937
- ² Edwards, E A Observations on Phlebitis *Am Heart Jour*, 14, 428, 1937
- ³ Edwards, E A, and Edwards, J A Effect of Thrombophlebitis on Venous Valve Surg, Gynec, and Obstet, 65, 310, 1937
- ⁴ Eisenklamm, I Operative Behandlung der akuten lokalisierten phlebitis der unteren Extremitäten *Wien klin Wchnschr*, 42, 360, 1929
- ⁵ Faxon, H H Treatment of Varicosities Preliminary High Ligation of the Internal Saphenous Vein with Injection of Sclerosing Solutions *Arch Surg*, 29, 794, 1934
- ⁶ Freeman, Walter Pulmonary Embolism Report of a Case *J A M A*, 97, 1624, 1931
- ⁷ Homans, J Thrombophlebitis of the Lower Extremities *ANNALS OF SURGERY*, 87, 641, 1928
- ⁸ Homans, J Venous Thrombosis in Lower Limbs Its Relation to Pulmonary Embolism *Am Jour Surg*, 38, 316, 1937
- ⁹ Nobl, G Prevention of Varicose Thrombophlebitis *Wien klin Wchnschr*, 49, 240, 1936
- ¹⁰ O'Neil, E E Thrombophlebitis in Varicose Veins *New Eng Jour Med*, 204, 1293, 1931
- ¹¹ Sears, J B Embolism from Saphenous Thrombophlebitis and Its Prophylaxis *New Eng Jour Med*, 212, 874, 1935
- ¹² Stone, H B Surgical Treatment of Postoperative Saphenous Thrombophlebitis *ANNALS OF SURGERY*, 96, 683, 1932

FINNEY-HOWELL RESEARCH FOUNDATION, INC

ANNOUNCEMENT has been made by the Finney-Howell Research Foundation, Inc, that all applications for fellowships for next year must be filed in the office of the Foundation, 1211 Cathedral Street, Baltimore, Md, by January 1, 1940. Applications received after that date cannot be considered for 1940 awards, which will be made the first of March, 1940.

This Foundation was provided for in the will of the late Dr George Walker of Baltimore for the support of "research work into the cause or causes and the treatment of cancer." The will directed that the surplus income from the assets of the Foundation together with the principal sum should be expended within a period of ten years to support a number of fellowships in cancer research, each with an annual stipend of two thousand dollars, "in such universities, laboratories and other institutions, wherever situated, as may be approved by the Board of Directors."

Fellowships carrying an annual stipend of \$2000 are awarded for the period of one year, with the possibility of renewal up to three years, when deemed wise by the Board of Directors, special grants of limited sums may be made to support the work carried on under a fellowship.

Applications must be made on the blank forms which will be furnished by the Secretary or any member of the Board of Directors.

October 16, 1939

CORRECTION

In the article by Dr John deJ Pemberton "Reactions Following Operations for Hyperthyroidism" *Annals of Surgery*, 104, 507-512, October, 1936, the concentration of sodium citrate was erroneously reported. The last four lines, page 512, should have read "In two of the cases of exophthalmic goiter marked clinical improvement apparently resulted from the intravenous administration of a solution of 0.5 per cent sodium citrate and 0.9 per cent sodium chloride to which was added an active preparation of cortin."

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M D
1833 Pine Street, Philadelphia, Pa

Contributions in a foreign language when accepted will be translated and published in English

Exchanges and Books for Review should be sent to James T. Pilcher, M D, Managing Editor, 121 Gates Avenue, Brooklyn, N Y

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
227 South Sixth Street, Philadelphia, Pa

INDEX TO VOLUME 110

A

ABBOTT, LEROY C Operative Lengthening of Tibia and Fibula, 961
 Abdominal Lesions, Circulatory Problems of Surgical Importance in Diagnosis of, 766, Surgery, Spinal Anesthesia in, 863
 Abscess, Left Subphrenic, 562
 Abscesses, Retropharyngeal and Lateral Pharyngeal, 177
 Acid, Dehydrocholic, Effect of, Upon Biliary Pressure and Its Clinical Application, 67
 Acoustic Neuromata, Total and Intracapsular Extirpation of, 513
 Acute Intestinal Obstruction, Effect of, on the Blood and Plasma Volumes, 25
 Address, Presidential, 481
 Adenocarcinoma of the Transverse Colon in a Boy Age Fifteen, 472
 Advantages, Demonstrable and Technic, of the Devine Colostomy, 14
 Agenesis, Unilateral, of Mullerian System in the Female, 316
 Agents, Assay of General Anesthetic, 823
 Air, Sterilization of, with Bactericidal Radiant Energy, 291.
 ALLEN, A W Control of Postoperative Bleeding in Obstructive Jaundice, 693
 American Board of Surgery, Report on, 1115
 Anesthesia, Intravenous and Regional, 878, Morphine and Cyclopropane, Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or, 84, Present Status of Spinal, 851, Spinal in Abdominal Surgery, 863, Spinal, for Thoracoplasty, Further Experiences in Use of, 872, Sympathetic Nerve Block as Adjunct, in Minimal Resection of Stomach for Peptic Ulcer, 886, Trends in Inhalation, 830
 Anesthetic Agents, Assay of General, 823
 Anesthetics and Drugs, Influence of Certain, Upon Gastro-intestinal Tone and Motility, 802
 Aneurysm, Arteriovenous, of the Neck, 131, of External Carotid Artery with Carotid Sinus Reflex, 133, Intracranial Arteriovenous, 525
 Ankle Malunion, Treatment of, 447
 Announcement of Third International Cancer Congress, 319
 Anovula 835
 Anus, Artificial, with Mechanical Sphincter, 311

Appendicitis, Acute, with Perforation, Primary Closure of Peritoneum in, 222, in Man, Experimental Proof of Obstructive Origin of, 629, Ruptured, Paratyphoid Fever Complicated by, 466
 Application of Carbamide (Urea) Therapy in Wound Healing, 94
 Arteries, Two Cystic, and Two Cystic Ducts, Double Gallbladder with, 60
 Arteriosus, Patent Ductus, Surgical Management of, 321
 Arteriovenous Aneurysms, Intracranial, 525, of the Neck, 131
 Artery, Aneurysm of External Carotid, with Carotid Sinus Reflex, 133, and Vein, Nutrient, Disruption of, Effect on Bone Marrow of, 940
 Artificial Anus with Mechanical Sphincter, 311
 Ascites, Chylous, 140, and Hydrothorax, Fibroma of the Ovary with, 731
 Assay of General Anesthetic Agents, 823
 Avulsed Skin Flaps, Treatment of, 951

B

Bactericidal Radiant Energy, Sterilization of Air with, 291
 BAILEY, FRED W Obituary of Francis Redei, 149
 Balance, Water and Electrolyte, Control of, in Surgical Patients, 1050
 BALFOUR, DONALD C Obituary of Sir Thomas Myles by, 790
 Barbiturates, Use of, in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, 84
 BARKER, M HERBERT Clinical and Experimental Experiences in the Surgical Treatment of Hypertension, 1016
 BARROW, D WOOLFOLK Fatal Pulmonary Embolism from Superficial Thrombophlebitis, 1118
 BARTLETT, WILLARD Obituary of Ellis Fischel, 156
 BAXTER, JAMES H, JR Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, 84
 BEECHER, HENRY K Assay of General Anesthetic Agents, 823
 BERNHARD, A Significance of Cholesterol Partition of Blood Serum in Surgery of the Gallbladder, 701
 BEST, R RUSSELL Effect of Dehydrocholic Acid Upon Biliary Pressure and Its Clinical Application, 67

- Bile Duct, Common, Primary Carcinoma of the, 474, Double Common, with Chole-
dochus Cyst, 55
- Bile from the Liver, Effect of Distention
of Colon and Stimulation of Its Nerve
Supply on Flow of, 755
- Biliary Fistulae, Internal, and Intestinal
Obstructions Due to Gallstones, 50,
Pressure and Its Clinical Application,
Effect of Dehydrocholic Acid Upon, 67
- BINNEY, HORACE Extrapleural Pneumo-
thorax, 578
- BISGARD, J DWLEY Influence of Certain
Drugs and Anesthetics Upon Gastro-
intestinal Tone and Motility, 802
- BLAIR, VILRAY P Obituary of John
Roberts Caulk, 151
- BLALOCK, ALFRED Myasthenia Gravis and
Tumors of Thymic Region, 544
- Bleeding, Control of Postoperative, in Ob-
structive Jaundice, 693
- Blood, and Plasma Volumes, Effect of
Acute Intestinal Obstruction on the, 25,
Serum in Surgery of the Gallbladder,
Significance of Cholesterol Partition of
the, 701
- Board of Surgery, American, Report on,
1115
- BOLDREY, EDWIN B Dermoid Cysts of the
Vertebral Canal, 273
- Bone, Solitary Myeloma of, 427, Marrow,
Effect on, of Disruption of Nutrient Ar-
tery and Vein, 940
- BOOK REVIEW Modern Surgical Technic
by MAX THOREK, Reviewed by Merrill N
Foote, 158, Operative Orthopedics by
Willis C Campbell, Reviewed by Robert
L Preston, 800, Surgical Pathology of
the Mouth and Jaws by Arthur E Hertz-
ler, Reviewed by Irving M Derby, 480
- BOOKS RECEIVED, 320
- BOURNE, WESLEY Further Experiences in
Use of Spinal Anesthesia for Thoraco-
plasty, 872, Trends in Inhalation Anes-
thesia, 830
- Bowel Obstruction in the New Born, 587
- BROWDER, JEFFERSON Reevaluation of
Treatment of Head Injuries, 357
- BROWN, W EASON Spinal Anesthesia in
Abdominal Surgery 863
- BUCHANAN, EDWIN P Chylous Ascites,
140
- Burrowing, Undermining, Chronic Ulcers
Due to the Micro-aerophilic Hemolytic
Streptococcus, Combined Use of Zinc
Peroxide and Sulfanilamide in Treat-
ment of, 1067
- BUSH, LEONARD F Present Status of
Spinal Anesthesia, 851
- Cancer Congress, Announcement of Third
International, 319
- Carbamide (Urea) Therapy, Application
of, in Wound Healing, 94
- Carcinoma, of the Colon and Rectum, 1,
Primary, of the Common Bile Duct, 474
- Cardiac Irregularities, Use of Barbiturates
in Preventing, Under Cyclopropane or
Morphine and Cyclopropane Anesthesia,
84
- Carotid Artery, Aneurysm of External,
with Carotid Sinus Reflex, 133
- CARP, LOUIS Fractures and Dislocations by
Muscular Violence Complicating Con-
vulsions Induced by Metrazol for Schizo-
phrenia, 107
- CARTER, BURR N Left Subphrenic Abscess,
562
- Cascara Sagrada, Melanosis Coli, An At-
tempt at Its Experimental Production
by Repeated Administration of, 461
- Cavernous Hemangioma of a Cervical
Nerve, 138
- Cecostomy as Complementary and Decom-
pressive Operation, 380
- Cervical Nerve, Cavernous Hemangioma
of a, 138
- CHERNEY, LEONID S Unilateral Agenesis
of the Mullerian System in the Female,
316
- Choledochus Cyst with Double Common
Bile Duct, 55
- Cholesterol Partition of the Blood Serum
in Surgery of the Gallbladder, Signifi-
cance of, 701
- Chondritis of Knee, 948
- Chronic Ulcers Due to Micro-aerophilic
Hemolytic Streptococcus, Combined Use
of Zinc Peroxide and Sulfanilamide in
Treatment of, 1067
- Chyle Cysts, Retroperitoneal, 389
- Chylous Ascites, 140
- Circulatory Problems of Surgical Impor-
tance in the Diagnosis of Abdominal Le-
sions, 766
- CLARK, DWIGHT E Significance of Lipo-
calc in Surgery, 907
- Clinical Consideration of Methods of
Equalizing Leg Length, 992, and Experi-
mental Experiences in the Surgical
Treatment of Hypertension, 1016
- Closure, Primary, of Peritoneum in Acute
Appendicitis with Perforation, 222
- Coli, Melanosis, 461
- Colon, Effect of Distention of the, and
Stimulation of Its Nerve Supply on Flow
of Bile from the Liver, 755, and Rectum
Carcinoma of the, 1, Transverse, Adeno-
carcinoma of the, in a Boy Age Fifteen,
472
- Colostomy, Devine, Technic and Demon-
strable Advantages of the, 14, Value of
Preliminary, in Correction of Gastro-
jejuno-colic Fistula, 659
- COLP, RALPH Ileocolostomy with Exclu-
sion, 648, Obituary of Edwin Beer by,
795

C

- CAMPBELL, WILLIS C Use of Vitallium as
Material for Internal Fixation of Frac-
tures, 119
- Canal, Vertebral Dermoid Cysts of the,
273

- Common Bile Duct, Double, with Choledochus Cyst, 55, Primary Carcinoma of the, 474
 Congenital Cystic Kidney Treated by Ureteral Drainage, 231
 Congress, Announcement of Third International Cancer, 319
 Contracture, Volkmann's Ischemic, Treatment of, 417
 Control, of Postoperative Bleeding in Obstructive Jaundice, 693, of Water and Electrolyte Balance in Surgical Patients, 1050
 Convulsions Induced by Metrazol for Schizophrenia, Fractures and Dislocations by Muscular Violence, Complicating, 107
 Correction, 480, of John Pemberton article, 1120
 CORWIN, WARREN C Melanosis Coli An Attempt at Its Experimental Production by Repeated Administration of Cascara Sagrada, 461
 Cranial Defects, Repair of, by Cranioplasty, 488
 Cranioplasty, Repair of Cranial Defects by, 488
 Cure of Flatfoot, Operation for, 437
 Cyclopropane, Use of Barbiturates in Preventing Cardiac Irregularities Under, or Morphine and Cyclopropane Anesthesia, 84
 Cyst, Choledochus with Double Common Bile Duct, 55, Spinal Extradural, Associated with Kyphosis Dorsalis Juvenilis, 285
 Cystic Ducts, Two, and Two Cystic Arteries, Double Gallbladder with, 60, Kidney, Congenital, Treated by Ureteral Drainage, 231
 Cysts, Dermoid, of the Vertebral Canal, 273, Retroperitoneal Chyle, 389
 Devine Colostomy, Technic and Demonstrable Advantages of the, 14
 Diabetic, Gangrene of the Extremity in the, 723
 Diagnosis of Abdominal Lesions, Circulatory Problems of Surgical Importance in, 766
 Digital Extensor Tendons, Habitual Dislocation of the, 81
 Discussion of Multiple Neurofibromatosis, 916
 Dislocation, Habitual, of the Digital Extensor Tendons, 81
 Dislocations and Fractures by Muscular Violence Complicating Convulsions Induced by Metrazol for Schizophrenia, 107
 Disruption of Nutrient Artery and Vein Effect on Bone Marrow of, 940
 Distention of the Colon, Effect of, and Stimulation of Its Nerve Supply on Flow of Bile from the Liver, 755
 Double Common Bile Duct, Choledochus Cyst with, 55, Gallbladder with Two Cystic Ducts and Two Cystic Arteries, 60
 DRAGSTEDT, LESTER R Significance of Lipocais in Surgery, 907
 Drainage, Ureteral, Congenital Cystic Kidney Treated by, 231
 Drugs and Anesthetics, Influence of Certain, Upon Gastro-intestinal Tone and Motility, 802
 Duct, Double Common Bile, with Choledochus Cyst, 55
 Ductus Arteriosus, Patent, Surgical Management of, 321
 Duodenal Ulcer, Study of Results of Medical Treatment of, 37
 Duodenal and Recurring Ulcer, Lateral Gastroduodenostomy in Cases of, 622

D

- DANDY, WALTER E Papilledema without Intracranial Pressure 161
 DARRACH, WILLIAM Chondritis of Knee, 948
 DAVIS, LOYAL Clinical and Experimental Experiences in the Surgical Treatment of Hypertension, 1016
 Decompressive and Complementary Operation, Cecostomy as, 380
 Defects, Repair of Cranial, by Cranioplasty, 488
 Dehydrocholic Acid, Effect of, Upon Biliary Pressure and Its Clinical Application, 67
 DENNIS, CLARENCE Experimental Proof of Obstructive Origin of Appendicitis in Man, 629
 DERBY IRVING M Review of Arthur E Hertzler's Surgical Pathology of the Mouth and Jaws, 480
 Dermoid Cysts of the Vertebral Canal 273
 Development of National Surgical Societies 481

E

- Effect of Acute Intestinal Obstruction on the Blood and Plasma Volumes, 25, on Bone Marrow of Disruption of Nutrient Artery and Vein, 940, of Dehydrocholic Acid Upon Biliary Pressure and Its Clinical Application, 67, of Distention of the Colon and Stimulation of Its Nerve Supply on Flow of Bile from the Liver, 755
 EGGERS, CARL Obituary of Franz J A Torek, by, 797
 Electrolyte and Water Balance, Control of, in Surgical Patients, 1050
 Electrosurgical Operation for Excision of a Hydrocele Sac 314
 ELKIN, D C Hurthle Cell Tumors of the Thyroid, 169
 ELKINTON, J RUSSELL Control of Water and Electrolyte Balance in Surgical Patients, 1050
 ELOESSER, LEO Obituary of Emmet Rixford, by 786
 ELTING, ARTHUR W Obituary of John Lawrence Yates by, 792

ELVIDGL, ARIHUR R Dermoid Cysts of the Vertebral Canal, 273
Embolism, Fat, 1095, Fatal Pulmonary, from Superficial Thrombophlebitis, 1118
Energy, Bactericidal Radiant, Sterilization of Air with, 291
Equalizing Leg Length, Clinical Consideration of the Methods of, 992
ESSER JOHANNIS F S An Artificial Anus with Mechanical Sphincter, 311
Evisceration Causing Rupture of Jejunum, 464
Excision of a Hydrocele Sac, Electrosurgical Operation for, 314
Exclusion, Ileocolostomy with, 648
Experiences, Clinical and Experimental, in the Surgical Treatment of Hypertension, 1016, in Use of Spinal Anesthesia for Thoracoplasty, 872
Experimental and Clinical Experiences in the Surgical Treatment of Hypertension, 1016, Proof of Obstructive Origin of Appendicitis in Man, 629
Extensor Tendons, Digital, Habitual Dislocation of the, 81
External Carotid Artery, Aneurysm of, with Carotid Sinus Reflex, 133
Extirpation, Total and Intracapsular, of Acoustic Neuromata, 513
Extradural Cyst, Spinal, Associated with Kyphosis Dorsalis Juvenilis, 285
Extrapleural Pneumothorax, 578
Extremity, Gangrene of the, in the Diabetic, 723

F

FARMER, ALFRED W Treatment of Avulsed Skin Flaps, 951
Fat Embolism, 1095
Fatal Pulmonary Embolism from Superficial Thrombophlebitis, 1118
Female, Mullerian System in the, Unilateral Agenesis of, 316
Fever, Paratyphoid Complicated by Ruptured Appendicitis, 466
Fibroma of the Ovary with Ascites and Hydrothorax, 731
Fibula and Tibia, Operative Lengthening of, 961
FINE, JACOB Effect of Acute Intestinal Obstruction on the Blood and Plasma Volumes, 25, The Role of the Nervous System in Acute Intestinal Obstruction, 411
FINLAYSON, ALISTER I Effect of Dehydrocholic Acid Upon Biliary Pressure and Its Clinical Application, 67
Finney-Howell Research Foundation, Inc Notice of, 1120
Fistula, Gastrojejunal, Value of Preliminary Colostomy in Correction of, 659
Fistulae, Internal Biliary, and Intestinal Obstructions Due to Gallstones, 50
FITZGERALD, R R Habitual Dislocation of the Digital Extensor Tendons, 81

FITZHUGH, O GARTH Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, 84
Fixation of Fractures, Internal, Use of Vitallium as Material for, 119
Flaps, Treatment of Avulsed Skin, 951
Flatfoot, Operation for Cure of, 437,
FLOOD, CHARLES A Study of Results of Medical Treatment of Duodenal Ulcer, 37
FOOTL, MILLER N Review of Modern Surgical Technique, by, 158
FOSS, HAROLD L Present Status of Spinal Anesthesia, 851
Fractures, and Dislocations by Muscular Violence Complicating Convulsions Induced by Metrazol for Schizophrenia, 107, Internal Fixation of, Use of Vitallium as Material for, 119

G

Gallbladder, Double, with Two Cystic Ducts and Two Cystic Arteries, 60, Surgery of the, Significance of Cholesterol Partition of the Blood Serum in, 701
Gallstones, Internal Biliary Fistulae and Intestinal Obstructions Due to, 50
Gangrene, Gas, 100, of the Extremity in the Diabetic, 723
GARIOCK, JOHN H Primary Carcinoma of the Common Bile Duct, 474
Gas Gangrene, 100
Gastrocolic Omentum and Transverse Mesocolon, Hernia Through, 456
Gastroduodenostomy, Lateral, in Cases of Duodenal and Recurring Ulcer, 622
Gastro-intestinal Tone and Motility, Influence of Certain Drugs and Anesthetics Upon, 802
Gastrojejunal Fistula, Value of Preliminary Colostomy in Correction of, 659
GINDLE, SAMUEL Effect of Acute Intestinal Obstruction on the Blood and Plasma Volumes, 25, The Role of the Nervous System in Acute Intestinal Obstruction, 411
General Anesthetic Agents, Assay of, 823
GERBODE, F Sclerosing or Retractable Mesenteritis, 669
GERSTER, JOHN C A Retroperitoneal Chyle Cysts with Reference to the Lymphangiomas, 389
GILMOUR, MONROE T Control of Water and Electrolyte Balance in Surgical Patients, 1050
GINZBURG, LEON Ileocolostomy with Exclusion, 648
Gland, Pituitary, Role of the, in Water Balance, 1037
GOLDMAN, LEON Effect of Distention of Colon and Stimulation of Its Nerve Supply on Flow of Bile from the Liver, 755

- GRAHAM, CHARLES P Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis, 285
GRAHAM, EVARTS A Report on American Board of Surgery, 1115
GRAHAM, ROSCOE R Spinal Anesthesia in Abdominal Surgery, 863
GRANT, FRANCIS C Repair of Cranial Defects by Cranioplasty, 488
Gravis, Myasthenia, and Tumors of Thymic Region, 544
GRODINSKY, MANUEL Retropharyngeal and Lateral Pharyngeal Abscesses, 177
GROSS, ROBERT E Surgical Management of Patent Ductus Arteriosus, 321
GURD, FRASER B Further Experiences in Use of Spinal Anesthesia for Thoracoplasty, 872

H

- Habitual Dislocation of the Digital Extensor Tendons, 81
HALFORD, F J Sclerosing or Retractable Mesenteritis, 669
HAMSA, WILLIAM R Treatment of Ankle Malunion, 447
HANFORD, JOHN M Aneurysm of External Carotid Artery with Carotid Sinus Reflex, 133, Arteriovenous Aneurysm of the Neck, 131, Cavernous Hemangioma of a Cervical Nerve, 138, Malignant Hemangio-Endothelioma of the Neck, 136
HARRIS, ROBERT I Fat Embolism, 1095
HART, DERYL A Discussion of Multiple Neurofibromatosis, 916, Postoperative Temperature Reactions, Reductions Obtained by Sterilizing the Air with Bactericidal Radiant Energy, 291
HARTMAN, F W Anoxia, 835
HARVEY, HAROLD D Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of Chronic, Undermining, Burrowing Ulcers Due to Micro-aerophilic Hemolytic Streptococcus, 1067
HAWKES, STUART Z Paratyphoid Fever Complicated by Ruptured Appendicitis, 466
Head Injuries, Revaluation of Treatment of, 357
HEINBECKER, PETER Role of the Pituitary Gland in Water Balance, 1037
HELWIG, FERDINAND C Liver Trauma and Hepatorenal Syndrome, 682
Hemangio-Endothelioma of the Neck, Malignant, 136
Hemangioma, Cavernous, of a Cervical Nerve, 138
Hemolytic Streptococcus, Micro-aerophilic, Chronic Ulcers Due to, Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of, 1067
Hemorrhage, Massive, in Peptic Ulcer, 376, Shock and Its Differentiation from, 260
Hepatorenal Syndrome and Liver Trauma, 682

- Hernia Through Transverse Mesocolon and Gastrocolic Omentum, 456
HICKEN, N FREDERICK Effect of Dehydrocholic Acid Upon Biliary Pressure and Its Clinical Application, 67
HINTON, J WILLIAM Massive Hemorrhage in Peptic Ulcer, 376
HODGL, EDWARD B The Samuel D Gross Prize Notice, 160
HOLDER, HALL G Application of Carbamide (Urea) Therapy in Wound Healing, 94
HORRAN, GILBERT Experiences with Total and Intracapsular Extirpation of Acoustic Neuromata, 513
HORSLEY, J SHILLTON Peptic Ulcers Perforating into the Pancreas, 606
HUGGINS, CHARLES Effect on Bone Marrow of Disruption of Nutrient Artery and Vein, 940

- HUNNER, GUY L Congenital Cystic Kidney Treated by Ureteral Drainage, 231
HUNT, VERNE C Lateral Gastroduodenostomy in Cases of Duodenal and Recurring Ulcer, 622
Hurthle Cell Tumors of the Thyroid, 109
Hydrocele Sac, Electrosurgical Operation for Excision of an, 314
Hydrothorax and Ascites, Fibroma of the Ovary with, 731
Hypertension, Clinical and Experimental Experiences in the Surgical Treatment of Hypertension, 1016

I

- Ileocolostomy with Exclusion, 648
Influence of Certain Drugs and Anesthetics Upon Gastro-intestinal Tone and Motility, 802
Inhalation Anesthesia, Trends in, 830
Injuries, Head, Revaluation of Treatment of, 357
Internal Biliary Fistulae and Intestinal Obstructions Due to Gallstones, 50, Fixation of Fractures, Use of Vitallium as Material for, 119
International Cancer Congress, Announcement of Third, 319
Intestinal Obstruction, Acute, Effect of, on the Blood and Plasma Volumes, 25, The Role of the Nervous System in, 411
Intestinal Obstructions and Internal Biliary Fistulae Due to Gallstones, 50
Intracapsular and Total Extirpation of Acoustic Neuromata, 513
Intracranial Arteriovenous Aneurysms, 525, Pressure, Papilledema without, 161
Intravenous and Regional Anesthesia, 878
Ischemic Contracture, Volkmann's, Treatment of, 417
IVY, A C Effect of Distention of Colon and Stimulation of Its Nerve Supply on Flow of Bile from the Liver, 755

J

- JACKSON, REGINALD H Technic and Demonstrable Advantages of the Devine Colostomy, 14
Jaundice, Obstructive, Control of Post-operative Bleeding in, 693
Jejunum, Rupture of, Evisceration Causing, 464
JOHNSON, E K Influence of Certain Drugs and Anesthetics Upon Gastrointestinal Tone and Motility, 802
JONES, RANDOLPH, JR Discussion of Multiple Neurofibromatosis, 916

K

- KENT, EDWARD M Value of Preliminary Colostomy in Correction of Gastrojejuno-colic Fistula, 659
Kidney, Congenital Cystic, Treated by Ureteral Drainage, 231
KLEINBERG, SAMUEL Traumatic Myositis Ossificans, 144
Knee, Chondritis of, 948
KOHN, IRVING L Significance of Cholesterol Partition of Blood Serum in Surgery of the Gallbladder, 701
KRUSEN, FRANK H Treatment of Volkmann's Ischemic Contracture, 417
Kyphosis Dorsalis Juvenilis, Spinal Extra-dural Cyst Associated with, 285

L

- LAHEY, FRANK H Carcinoma of the Colon and Rectum, 1
Lateral Gastroduodenostomy in Cases of Duodenal and Recurring Ulcer, 622, Pharyngeal and Retropharyngeal Abscesses, 177
LEAMAN, WM G Circulatory Problems of Surgical Importance in Diagnosis of Abdominal Lesions, 766
Left Subphrenic Abscess, 562
Leg Length, Equalizing, Clinical Consideration of the Methods of, 992
LEHMAN, EDWIN P Obituary of John Henry Neff, Jr, 153
Lengthening, Operative, of Tibia and Fibula, 961
Lesions, Abdominal, Circulatory Problems of Surgical Importance in Diagnosis of, 766
Lipocarcinoma in Surgery, Significance of, 907
Liver, Flow of Bile from, Effect of Distention of Colon and Stimulation of Its Nerve Supply on, 755 Trauma and Hepatorenal Syndrome, 682
LOEB, SAM A An Electrosurgical Operation for Excision of an Hydrocele Sac, 314
LUNDY, JOHN S Intravenous and Regional Anesthesia, 878
Lymphangiomata with Reference to Retroperitoneal Chyle Cysts, 389
Lymphosarcoma, Primary of the Stomach, 200

M

- MACGUIRL, CONSTANTINE J Adenocarcinoma of the Transverse Colon in a Boy Age Fifteen, 472
MACKAY, EATON M Application of Carbamide (Urea) Therapy in Wound Healing, 94
MACLACHLIN, ANGUS Fat Embolism, 1095
Malignant Hemangio-Endothelioma of the Neck, 136
Malunion, Treatment of Ankle, 447
Management, Surgical, of Patent Ductus Arteriosus, 321
MARTIN, J D, JR Hurthle Cell Tumors of the Thyroid, 169
MASON, M F Myasthenia Gravis and Tumors of Thymic Region, 544
Massive Hemorrhage in Peptic Ulcer, 376
McCLURE, ROY D Anoxia, 835
MCQUEENEY, ANDREW M Internal Biliary Fistulae and Intestinal Obstructions Due to Gallstones, 50
Mechanical Sphincter, Artificial Anus with, 311
Medical Treatment of Duodenal Ulcer, Study of Results of, 37
MEIGS, JOE VINCENT Fibroma of the Ovary with Ascites and Hydrothorax, 731
Melanosis Coli, 461
MELENEY, FRANK L Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of Chronic, Undermining, Burrowing Ulcers Due to Micro-aerophilic Hemolytic Streptococcus, 1067
Mesenteritis, Sclerosing or Retractable, 669
Mesocolon Transverse and Gastrocolic Omentum, Hernia Through, 456
Methods of Equalizing Leg Length, Clinical Consideration of the, 992
Metrazol for Schizophrenia, Fractures and Dislocations by Muscular Violence Complicating Convulsions Induced by, 107
MEYERDING, HENRY W Treatment of Volkmann's Ischemic Contracture, 417
MEYERS, RUSSELL Reevaluation of Treatment of Head Injuries, 357
Micro-Aerophilic Hemolytic Streptococcus, Chronic Ulcers Due to, Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of, 1067
MILLER, EDWIN M Bowel Obstruction in New Born, 587
Minimal Resection of Stomach for Peptic Ulcer, Sympathetic Nerve Block as Adjunct Anesthesia in, 886
MITCHELL, CHARLES F The Samuel D Gross Prize Notice 160
MOCK, HARRY E Evisceration Causing Rupture of Jejunum, 464
MOON, VIRGIL H Early Recognition of Shock and Its Differentiation from Hemorrhage, 260
MORGAN, HUGH J Myasthenia Gravis and Tumors of Thymic Region, 544

Morphine and Cyclopropane Anesthesia, Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or, 84
Motility and Tone, Gastro-intestinal, Influence of Certain Drugs and Anesthetics Upon, 802
Mullerian System in the Female, Unilateral Agensis of, 316
Multiple Neurofibromatosis, Discussion of, 916
Muscular Violence, Fractures and Dislocations by, Complicating Convulsions Induced by Metrazol for Schizophrenia, 107
Myasthenia Gravis and Tumors of the Thymic Region, 544
Myeloma of Bone, Solitary, 427
Myositis Ossificans, Traumatic, 144

N

National Surgical Societies, Development of, 481
Neck, Arteriovenous Aneurysm of the, 131
Malignant Hemangio-Endothelioma of the, 136
Nerve Block, Sympathetic, as Adjunct Anesthesia in Minimal Resection of Stomach for Peptic Ulcer, 886
Nerve, Cervical, Cavernous Hemangioma of a, 138, Supply on Flow of Bile from the Liver, Effect of Distention of Colon and Stimulation of Its, 755
Nervous System, Rôle of the, in Acute Intestinal Obstruction, 411
Neuritis, Optic, 161
Neurofibromatosis, Discussion of Multiple, 916
Neuromata, Acoustic, Total and Intracapsular Extirpation of, 513
New Born, Bowel Obstruction in the, 587
NEWELL, E DUNBAR Gas Gangrene, 100
NORCROSS, NATHAN C Repair of Cranial Defects by Cranioplasty, 488
Nutrient Artery and Vein, Disruption of, Effect on Bone Marrow of, 940

O

Obituary Beer, Edwin, by Ralph Colp, 795
Caulk, John Roberts, by Wilray P. Blain, 151, Fischel, Ellis, by Willard Bartlett, 156, Myles, Sir Thomas, by Donald C Balfour, 790, Neff, John Henry, Jr., by Edwin P. Lehman, 153, Reder, Francis, by Fred W. Bailey, 149, Rixford, Emmet, by Leo Eloesser, 786, Torek, Franz J. A., by Carl Eggers, 797, Yates, John Lawrence, by Arthur W. Elting, 792
Obstruction, Acute Intestinal, Effect of, on the Blood and Plasma Volumes, 25, Acute Intestinal, The Rôle of the Nervous System, 411, Bowel, in the New Born, 587, Intestinal, and Internal Biliary Fistulas Due to Gallstones, 50

Obstructive Jaundice, Control of Post-operative Bleeding in, 693, Origin of Appendicitis in Man, Experimental Proof of, 629
Omentum, Gastrocolic and Transverse Mesocolon, Hernia Through, 456
Operation, Complementary and Decompressive, Cecostomy as, 380, for Cure of Flatfoot, 437, Electrosurgical, for Excision of a Hydrocele Sac, 314
Operative Lengthening of Tibia and Fibula, 961
Optic Neuritis, 161
Origin, Obstructive, of Appendicitis in Man, Experimental Proof of, 629
ORDORFF, JOHN R Evisceration Causing Rupture of Jejunum, 464
ORR, THOMAS G Liver Trauma and Hepatorenal Syndrome, 682
Ossificans, Myositis, Traumatic, 144
Ovary, Fibroma of the, with Ascites and Hydrothorax, 731

P

Pancreas, Peptic Ulcers Perforating into the, 606
Papilledema without Intracranial Pressure, 161
Paratyphoid Fever Complicated by Ruptured Appendicitis, 466
Partition, Cholesterol, of the Blood Serum in Surgery of the Gallbladder, Significance of, 701
PASTERNAK, JOSEPH G Solitary Myeloma of Bone, 427
Patent Ductus Arteriosus, Surgical Management of, 321
Patients, Surgical, Control of Water and Electrolyte Balance in, 1050
PEMBERTON, JOHN DEJ Correction of article by, 1120
Peptic Ulcer, Massive Hemorrhage in, 376, Perforating into the Pancreas, 606, Sympathetic Nerve Block as Adjunct Anesthesia in Minimal Resection of Stomach for, 886
Peritoneum, Primary Closure of, in Acute Appendicitis with Perforation, 222
PERRETT, T S Fat Embolism, 1095
PFEIFFER, DAMON B Value of Preliminary Colostomy in Correction of Gastro-jejunal Colic Fistula, 659
Pharyngeal, Lateral and Retropharyngeal Abscesses, 177
PHEMISTER, DALLAS B Presidential Address, Development of National Surgical Societies, 481, Valedictory, 960
PICKHARDT, OTTO C Significance of Cholesterol Partition of Blood Serum in Surgery of the Gallbladder, 701
Pituitary Gland in Water Balance, Rôle of the, 1037
Plasma and Blood Volumes, Effect of Acute Intestinal Obstruction on the, 25
Pneumothorax, Extrapleural, 578

- POPPEN, JAMES L Experiences with Total and Intracapsular Extirpation of Acoustic Neuromata, 513
Postoperative Bleeding in Obstructive Jaundice, Control of, 693, Temperature Reactions, 291
Preliminary Colostomy, Value of, in Correction of Gastrojejunocolic Fistula, 659
Present Status of Spinal Anesthesia, 851
Presidential Address, 481
Pressure, Biliary, and Its Clinical Application, Effect of Dehydrocholic Acid Upon, 67, Intracranial, Papilledema without, 161
PRESTON, ROBERT L Review of Operative Orthopedics by, 800
Primary Carcinoma of the Common Bile Duct, 474, Closure of Peritoneum in Acute Appendicitis with Perforation, 222, Lymphosarcoma of the Stomach, 200
Problems, Circulatory, of Surgical Importance in the Diagnosis of Abdominal Lesions, 766
Proof, Experimental, of Obstructive Origin of Appendicitis in Man, 629
Pulmonary Embolism, Fatal, from Superficial Thrombophlebitis, 1118

R

- Radiant Energy Bactericidal, Sterilization of Air with, 291
RANKIN, FRED W Value of Cecostomy as Complementary and Decompressive Operation, 380
Reactions, Postoperative Temperature, 291
Rectum and Colon, Carcinoma of the, 1
Recurring and Duodenal Ulcer, Lateral Gastroduodenostomy in Cases of, 622
Regional and Intravenous Anesthesia, 878
REICHERT, F L Sclerosing or Retractable Mesenteritis, 669
Repair of Cranial Defects by Cranioplasty, 488
Report on the American Board of Surgery, 1115
Resection of Stomach for Peptic Ulcer, Minimal, Sympathetic Nerve Block as Adjunct Anesthesia in, 886
Results of Medical Treatment of Duodenal Ulcer, Study of, 37
Retractable or Sclerosing Mesenteritis, 669
Retroperitoneal Chyle Cysts, 389
Retropharyngeal and Lateral Pharyngeal Abscesses, 177
Revaluation of Treatment of Head Injuries, 357
RIENHOFF, WM F, JR Sympathetic Nerve Block as Adjunct Anesthesia in Minimal Resection of Stomach for Peptic Ulcer, 886
RIVEN, S S Myasthenia Gravis and Tumors of Thymic Region, 544

- ROBBINS, BENJAMIN H Use of Barbiturates in Preventing Cardiac Irregularities Under Cyclopropane or Morphine and Cyclopropane Anesthesia, 84
ROBERTSON, JAMES F Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis, 285
RODMAN, J STEWART Circulatory Problems of Surgical Importance in Diagnosis of Abdominal Lesions, 766
Role of the Nervous System in Acute Intestinal Obstruction, 411, of the Pituitary Gland in Water Balance, 1037
ROSENFELD, LOUIS The Role of the Nervous System in Acute Intestinal Obstruction, 411
ROURKE, G M Control of Postoperative Bleeding in Obstructive Jaundice, 693
Rupture of Jejunum, Evisceration Causing, 464
Ruptured Appendicitis, Paratyphoid Fever Complicated by, 466

S

- Sac, Hydrocele, Electrosurgical Operation for Excision of an, 314
ST JOHN, FORDYCE B Study of Results of Medical Treatment of Duodenal Ulcer, 37
SAMUEL D GROSS PRIZE NOTICE, 160
SAUNDERS, JOHN B DEC M Operative Lengthening of Tibia and Fibula, 961
SCHELLING, VICTOR Anoxia, 835
SCHNEDORF, J G Anoxia, 835
SCHOOLFIELD, BEN L An Operation for Cure of Fatfoot, 437
Sclerosing or Retractable Mesenteritis, 669
SHELLEY, HAROLD J Hernia Through Transverse Mesocolon and Gastrocolic Omentum, 456
Shock and Its Differentiation from Hemorrhage, 260
Significance of Cholesterol Partition of the Blood Serum in Surgery of the Gallbladder, 701, of Lipocac in Surgery, 907
SINGLETON, ALBERT O Intracranial Arteriovenous Aneurysms, 525
Sinus Reflex Aneurysm of External Carotid Artery with Carotid, 133
Skin Flaps, Treatment of Avulsed, 951
SMYTH, CALVIN M, JR The Samuel D Gross Prize Notice 160
Solitary Myeloma of Bone 427
SPEED, J S Use of Vitallium as Material for Internal Fixation of Fractures, 119
Sphincter, Mechanical, Artificial Anus with, 311
Spinal Anesthesia in Abdominal Surgery, 863, Present Status of, 851, for Thoracoplasty, Further Experiences in Use of, 872
Spinal Extradural Cyst Associated with Kyphosis Dorsalis Juvenilis, 285
Sterilization of Air with Bactericidal Radiant Energy, 291

STEWART, J D Control of Postoperative Bleeding in Obstructive Jaundice, 693
Stimulation of Its Nerve Supply on Flow of Bile from the Liver, Effect of Distention of the Colon and, 755
Stomach, Minimal Resection of, for Peptic Ulcer, Sympathetic Nerve Block as Adjunct Anesthesia in, 886, Primary Lymphosarcoma of the, 200
Streptococcus, Micro-aerophilic Hemolytic, Chronic Ulcers Due to, Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of 1067
Study of Results of Medical Treatment of Duodenal Ulcer, 37
Subphrenic Abscess, Left, 562
Sulfanilamide and Zinc Peroxide in Treatment of Chronic, Undermining, Burrowing Ulcers Due to Micro-aerophilic Hemolytic Streptococcus, 1067
Superficial Thrombophlebitis, Fatal Pulmonary Embolism from, 1118
Surgery, Abdominal, Spinal Anesthesia in, 863, American Board of, Report on, 1115, of the Gallbladder, Significance of Cholesterol Partition of the Blood Serum in, 701, Significance of Lipocaine in, 907
Surgical Importance in Diagnosis of Abdominal Lesions, Circulatory Problems of, 766, Management of Patent Ductus Arteriosus, 321, Patients, Control of Water and Electrolyte Balance in, 1050, Societies, National, Development of, 481, Treatment of Hypertension, Clinical and Experimental Experiences in the, 1016
SUSSMAN, MARCY Ileocolostomy with Exclusion, 648
Sympathetic Nerve Block as Adjunct Anesthesia in Minimal Resection of Stomach for Peptic Ulcer, 886
Syndrome, Hepatorenal, and Liver Trauma, 682

T

TAYLOR, EARL S Primary Lymphosarcoma of the Stomach, 200
Technic and Demonstrable Advantages of the Devine Colostomy, 14
Temperature, Postoperative, Reactions, 291
Tendons, Digital Extensor, Habitual Dislocation of the, 81
Third International Cancer Congress, Announcement of, 319
THOMPSON T CAMPBELL Clinical Consideration of the Methods of Equalizing Leg Length, 902
Thoracoplasty Spinal Anesthesia for, Further Experiences in Use of 872
Thrombophlebitis Superficial, Fatal Pulmonary Embolism from, 1118
Thymic Region, Tumors of, and Myasthenia Gravis 544
Thyroid, Hurthle Cell Tumors of the 169
Tibia and Fibula Operative Lengthening of 961

Tone and Motility, Gastro-intestinal, Influence of Certain Drugs and Anesthetics Upon, 802
Total and Intracapsular Extirpation of Acoustic Neuromata, 513
Transverse Colon, Adenocarcinoma of the, in a Boy Age Fifteen, 472, Mesocolon and Gastrocolic Omentum, Hernia through, 456
Trauma, Liver and Hepatorenal Syndrome, 682
Traumatic Myositis Ossificans, 144
Treatment of Ankle Malunion, 447, of Avulsed Skin Flaps, 951, of Head Injuries, Reevaluation of, 357, Medical, of Duodenal Ulcer, Study of Results of, 37, Surgical, of Hypertension, Clinical and Experimental Experiences in the, 1016, of Volkmann's Ischemic Contracture, 417
Trends in Inhalation Anesthesia, 830
Tumors, of Thymic Region and Myasthenia Gravis, 544, of the Thyroid, Hurthle Cell, 169
Two Cystic Ducts and Two Cystic Arteries, Double Gallbladder with, 60

U

Ulcer, Duodenal, and Recurring, Lateral Gastroduodenostomy in Cases of, 622, Study of Results of Medical Treatment of, 37
Ulcer, Minimal Resection of Stomach for Peptic, Sympathetic Nerve Block as Adjunct Anesthesia in, 886, Peptic, Massive Hemorrhage in, 376, Perforating into the Pancreas, 606
Undermining, Burrowing, Chronic Ulcers Due to the Micro-aerophilic Hemolytic Streptococcus, Combined Use of Zinc Peroxide and Sulfanilamide in Treatment of, 1067
Unilateral Agenesis of Mullerian System in the Female, 316
UPCHURCH, S E Postoperative Temperature Reactions, Reductions Obtained by Sterilizing the Air with Bactericidal Radiant Energy, 291
Urea (Carbamide Therapy) Application of, in Wound Healing, 94
Ureteral Drainage, Congenital Cystic Kidney Treated by, 231
Use of Vitallium as Material for Internal Fixation of Fractures, 119

V

Valedictory by President, Dallas B Phemister, 960
Value of Cecostomy as Complementary and Decompressive Operation, 380, of Preliminary Colostomy in Correction of Gastrojejunal Fistula, 659
Vein and Artery, Nutrient, Disruption of, Effect on Bone Marrow of, 940
VERMEULEN, C Significance of Lipocaine in Surgery, 907

- Vertebral Canal, Dermoid Cysts of the, 273
VINEBERG, A M Further Experiences in Use of Spinal Anesthesia for Thoracoplasty, 872
Vitalium, Use of, as Material for Internal Fixation of Fractures, 119
Volkman's Ischemic Contracture, Treatment of, 417
Volumes, Blood and Plasma, Effect of Acute Intestinal Obstruction on the, 25
Von Recklinghausen's Disease, 916

W

- WAGLSTEEN, OWEN H Experimental Proof of Obstructive Origin of Appendicitis in Man, 629
WARRLN, RICHARD Primary Closure of Peritoneum in Acute Appendicitis with Perforation, 222
Water Balance, Role of the Pituitary Gland in, 1037, and Electrolyte Balance, Control of, in Surgical Patients, 1050
WAUGH, RICHEY L Solitary Meloma of Bone, 427
WEEDER, S DANA Choledochus Cyst with Double Common Bile Duct, 55
WHITE, HARVEY L Role of the Pituitary Gland in Water Balance, 1037
WILGE, EUGENE Effect on Bone Marrow of Disruption of Nutrient Artery and Vein, 940
WILSON, CLAUDE L Double Gallbladder with Two Cystic Ducts and Two Cystic Arteries, 60
WILSON, PHILIP D Clinical Consideration of the Methods of Equalizing Leg Length, 992
WOLFF, WILLIAM A Control of Water and Electrolyte Balance in Surgical Patients, 1050
Wound Healing, Application of Carbamide (Urea) Therapy in, 94
WRIGHT, LOUIS T An Electrosurgical Operation for Excision of an Hydrocele Sac, 314

Z

- ZIRROLD, ARTHUR A Gangrene of the Extremity in the Diabetic, 723
Zinc Peroxide and Sulfanilamide in Treatment of Chronic, Undermining, Burrowing Ulcers Due to Micro-aerophilic Hemolytic Streptococcus, 1067

